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# SIX YEARS' EXPERIENCE OF THE THYROID SERVICE AT THE MASSACHUSETTS MEMORIAL HOSPITALS*

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BOSTON

THE Thyroid Service, which was established at the Massachusetts Memorial Hospitals in January, 1936, includes representatives of the associated specialties of otolaryngology and ophthalmology, as well as internists, cardiologists and surgeons. Up to January 1, 1942, the four surgeons on the Thyroid Service, the rotating residents and house staffs have performed three hundred and thirty-four thyroid operations on 288 patients, with 6 deaths, only 1 death having occurred in the last three years (Table 1). The operative mortality was 1.8 per cent, and the patient mortality 2.1 per cent. A review of the operative results has been of value, especially to the surgeons who have served on the hospital and outpatient thyroid services throughout this six-year period, in a realization of what has or has not been accomplished and of plans for future betterment.

Of the entire series, the ratio of females to males was 5.3 : 1. The youngest patient (exophthalmic goiter) was fifteen years old, and the oldest (carcinoma) seventy-one. Figure 1 shows the age distribution by decades for the toxic and nontoxic groups. As one would expect, exophthalmic goiter is a disease of youth, and nodular goiter one of older patients.

## HYPERTHYROIDISM

### *Exophthalmic Goiter*

One hundred and seventy-six operations were performed on 139 patients, with 3 fatalities, the operative mortality being 1.7 per cent. There were 105 females and 32 males, a ratio of 3.3 : 1. Eighteen of the 30 thyrocardiac cases occurred in the exophthalmic group (Table 1). A patient is described as thyrocardiac when he presents evidence of underlying cardiac damage associated with hyperthyroidism. Rheumatic, hypertensive and syphilitic heart diseases are most commonly found to be the cause of this damage. Impairment of the cardiac reserve is usually manifested by the presence of preoperative auricular fibrillation or cardiac decompensation, or both. These patients are much more serious operative risks, and all 18 were subjected to a two-stage thyroidectomy, with an interval of six weeks between operations. Two of the three deaths in the exophthalmic group occurred in known thyrocardiac patients, both after the first-stage hemithyroidectomy.

Experience has convinced us beyond doubt that subtotal thyroidectomy in the patient who is a poor risk may be too strenuous a procedure for him to withstand. This is especially true on a teaching service, where the operation may occasionally be prolonged. Therefore, objective evaluation of the patient on the basis of age, weight loss, duration of disease and response to treatment§ was adhered to in the selection of the operative procedure for each patient. Thus, in the exophthalmic group, 37 per cent of the patients were subjected to a two-stage thyroidectomy. All 3 fatalities in the exophthalmic group occurred during the first three years of the Thyroid Service, and after a first-stage hemithyroidectomy, an indication that all the patients were evaluated preoperatively as serious risks.

Twelve patients developed sufficiently severe postoperative reactions to be classified as suffering from thyroid storm, which, on the Thyroid Service, means the presence of a progressively rising fever and a rapid pulse rate, with or without irregularity, in addition to restlessness, delirium, pulmonary congestion and, in cases that cannot be controlled, a fatal ending. Again, on the basis of objective findings, all 12 patients had given enough preoperative warning, so that only a hemi-

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§Clute, H. M. Operative mortality in hyperthyroidism. *J. A. M. A.* 95:389-392, 1930.

thyroidectomy was carried out in any case. This storm, or rather thyroid crisis, was the major factor in the 3 fatalities, whereas the remaining 9 patients recovered. None of the patients selected for single-stage thyroidectomy developed postoperative storm.

The absence of mortality during the last three years is not explained, we believe, by any increase in the number of two-stage operations, for this

TABLE 1. *Summary of Cases of Hyperthyroidism.*

| YEAR | TOTAL NO. OF CASES | NO. OF CASES WITH THYROCARDIAC DISEASE | ONE-STAGE OPERATIONS | TWO-STAGE OPERATIONS | NO. OF DEATHS | OPERATIVE MORTALITY |
|---|---|---|---|---|---|---|
| | | | | | | % |
| Exophthalmic goiter | | | | | | |
| 1936 | 22 | 2 | 16 | 6 | 0 | 0 |
| 1937 | 29 | 7 | 19 | 10 | 2 | 7 |
| 1938 | 27 | 6 | 13 | 14 | 1 | 4 |
| 1939 | 25 | 2 | 14 | 11 | 0 | 0 |
| 1940 | 20 | 0 | 14 | 6 | 0 | 0 |
| 1941 | 16 | 1 | 12 | 4 | 0 | 0 |
| Totals | 139 | 18 | 88 | 51 (36.7%) | 3 | |
| Average | | | | | | 1.7 |
| Adenomatous goiter with hyperthyroidism | | | | | | |
| 1936 | 2 | 1 | 0 | 2 | 1 | 50 |
| 1937 | 7 | 2 | 6 | 1 | 0 | 0 |
| 1938 | 5 | 2 | 3 | 2 | 0 | 0 |
| 1939 | 6 | 1 | 6 | 0 | 0 | 0 |
| 1940 | 11 | 2 | 10 | 1 | 0 | 0 |
| 1941 | 9 | 1 | 8 | 1 | 1 | 11 |
| Totals | 40 | 9 | 33 | 7 | 2 | |
| Average | | | | | | 4.3 |
| Recurrent hyperthyroidism (exophthalmic — 15, adenomatous — 3) | | | | | | |
| 1936 | 1 | 0 | 1 | 0 | 0 | 0 |
| 1937 | 5 | 1 | 4 | 1 | 0 | 0 |
| 1938 | 1 | 0 | 1 | 0 | 0 | 0 |
| 1939 | 5 | 1 | 5 | 0 | 0 | 0 |
| 1940 | 3 | 0 | 3 | 0 | 0 | 0 |
| 1941 | 3 | 1 | 2 | 1 | 0 | 0 |
| Totals | 18 | 3 | 16 | 2 | 0 | |
| Average | | | | | | 0 |

percentage has remained essentially unchanged (Table 1). One reason for these better results is that 15 of the 18 thyrocardiac patients were operated on before 1938. However, there is a distinct impression throughout the Thyroid Service that measures of anticipating and combating postoperative thyroid storm at its inception have been continually intensified on our part. The longer preparation of cases for surgery and the increased use of the oxygen tent immediately after operation, in addition to adequately large doses of morphine, the preoperative use of fluids and glucose and the active aid of the internist and cardiologist, have resulted, we believe, in more effective control of the seriously ill patient.

Regarding complications in the exophthalmic group, no patient developed postoperative hemorrhage. The one wound infection of the entire series occurred in this group, following gross contamination of the wound at operation by soot from a backfiring ventilator. Three patients in this group sustained unilateral recurrent laryngeal-nerve injury; one such injury had cleared entirely

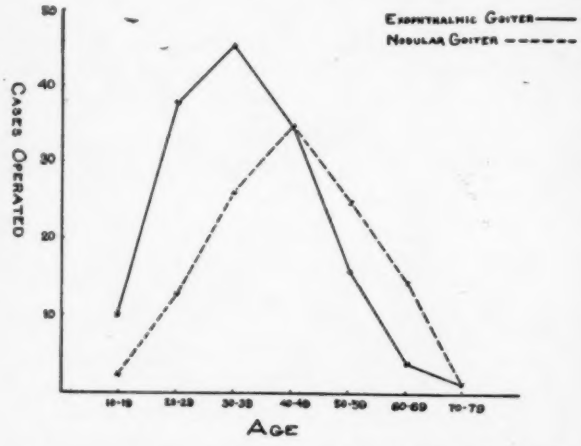


FIGURE 1. *Frequency of Operations for Exophthalmic Goiter and Nodular Goiter according to Age.*

when the larynx was examined four months later. The remaining two injuries were permanent, giving an incidence of 1.1 per cent in the one hundred and seventy-six operations performed in this

TABLE 2. *Complications in Three Hundred and Thirty-four Operations.*

| COMPLICATION | NO. OF CASES |
|---|---|
| Thyroid crisis (4 deaths) | 16 |
| Hypothyroidism | 12 |
| Nerve injury (unilateral) | 7 |
| Permanent | 4 |
| Transient | 3 |
| Hypoparathyroidism | 2 |
| Postoperative hemorrhage (recovery after reoperation) | 1 |
| Death on operating table (after fourteen minutes of operation) | 1 |
| Wound infection (contamination by soot at operation) | 1 |
| Psychosis (sixth day) | 1 |
| Atelectasis | 1 |
| Parotitis | 1 |
| Subconjunctival hemorrhage | 1 |
| Malignant exophthalmos (two-stage Naffziger operation) | 1 |
| Severe epistaxis (purpura hemorrhagica) | 1 |
| Acute cholecystitis (fifth day) | 1 |
| Catarrhal jaundice (third day) | 1 |

group. We do not routinely expose the recurrent laryngeal nerve in this clinic.

One patient developed clinical tetany from hypoparathyroidism on the sixth day after a second-stage thyroidectomy. Thirteen months later, dihydrotachysterol (AT 10) was still necessary for control of the patient's mild but definite symptoms.

Eleven of these 139 patients, or 8.0 per cent, developed recurrent hyperthyroidism, of whom 5

underwent reoperation and 6 preferred to delay. Five additional patients showed mild symptoms of recurrence, not sufficient to demand reoperation. Thus, if these 16 patients are regarded as having recurrent hyperthyroidism, the rate of recurrrence is 11.5 per cent.

Eight patients, or 5.7 per cent, known to have developed postoperative hypothyroidism, with clinical signs of myxedema, required oral thyroid therapy. Disclosure of a somewhat higher rate may result from follow-up of the patients more recently operated on.

One patient developed such severe epistaxis on the first postoperative day that anterior and posterior nasal packing was required. This twenty-one-year-old girl recovered normally thereafter, and was dismissed on the seventh postoperative day. Two months later, she developed extensive petechiae, followed by sudden nausea, vomiting, abdominal cramps, marked distention and severe pallor. She was readmitted to the Evans Memorial and, despite transfusions of blood, died within twenty-four hours. Autopsy revealed the cause of death to be intra-abdominal hemorrhage (5000 cc. of blood) from a ruptured corpus hemorrhagicum of the right ovary, with underlying purpura hemorrhagica.

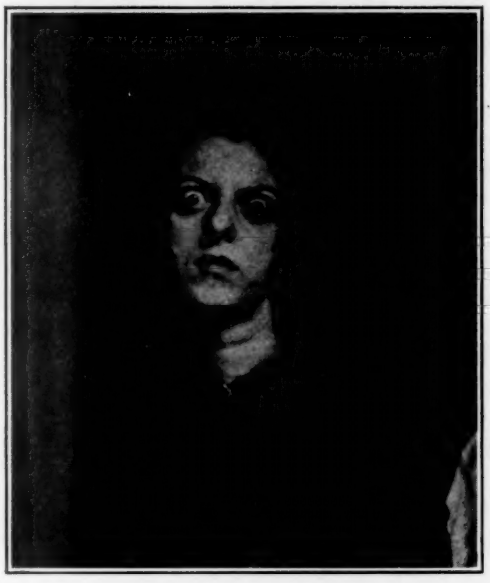

FIGURE 2.

*Appearance of a patient with progressive exophthalmos nine months after a two-stage thyroidectomy; the metabolism was normal.*

One patient developed a postoperative psychosis on the sixth day, and transfer to an institution for mental cases was necessary.

Progressive malignant exophthalmos after thyroidectomy was observed in 1 patient (Fig. 2). Four months after operation, the exophthalmos had visibly increased, despite apparent complete control of the hyperthyroidism. At eight months, vision became so blurred that the patient could not recognize her children across the room. She complained of increased lacrimation, diplopia, inflamed sore eyeballs and frequent sties. Efforts to protect the cornea by denuding and suturing together the lateral margins of the upper and lower eyelids for 8 mm. were unsuccessful. This was followed by removal of the bony roof of the right orbit (operation performed by Drs. Donald Munro and Walter R. Wegner), according to the Naffziger method. Twenty to thirty per cent recession of the eyeball resulted, with improved vision and relief of discomfort. Decompression of the left orbital roof was later done elsewhere. When the patient was seen one month after the second operation, there were definite relief of eye symptoms and improvement of vision.

The 3 fatal cases among the 139 patients with exophthalmic goiter are presented below.

CASE 1. Mrs. M. S., a 49-year-old Polish-American housewife, was admitted to the hospital on September 8, 1937. She had noticed swelling of the neck for 6 months and severe symptoms of hyperthyroidism for 2 months. Despite Lugol's solution, 8 minims three times a day, for 1 month, the symptoms were unabated. There was daily vomiting for 2 weeks, but no diarrhea or ankle edema. The patient had lost 14 pounds in a year.

Examination revealed a well-developed and well-nourished woman who showed marked activation. There was no exophthalmos or eye stare. The thyroid gland was firm, hyperplastic and symmetrically enlarged to four times the normal size. The heart was enlarged to the left and was fibrillating at a rate of 120 to 140 beats per minute; there was a pulse deficit of 50 at the wrist. The blood pressure was 130/80. The liver edge was palpable, but there was no ascites.

The basal metabolic rate was +19 per cent on admission, but 8 days later it was +49 per cent and the patient had lost an additional 8 pounds despite hospital care. The blood cholesterol was 147 mg. per 100 cc. After 13 days on iodine, bed rest and sedation, the patient had lost a total of 10 pounds, and the basal metabolic rate remained at +48 per cent. Under digitalis therapy, the cardiac rhythm became regular until the day of operation, when fibrillation recurred.

On the 14th day, a right hemithyroidectomy was performed, requiring 25 minutes. The patient's condition was satisfactory for 12 hours. Then, she became hyperactive and cyanotic. The temperature rose to 104°F., and the irregular pulse rate to 168, despite 33 gr. of digitalis in the preceding 12 days. Notwithstanding oxygen therapy, intravenous iodine, glucose, digitalis and heavy sedation, the patient became comatose, and died 39 hours after operation. The immediate cause of death was postoperative thyroid crisis. Permission for autopsy was not granted.

This patient had entered the hospital on the verge of thyroid crisis. Her failure to improve after fourteen days of medical management prompted the decision to intervene with hemithyroidectomy

in an attempt to arrest the uncontrolled hyperthyroidism. Viewed in retrospect, either preliminary bilateral superior-pole ligation or, even better, a much longer preoperative period might have favorably altered the outcome. The patient had received iodine for one month before admission, and this was perhaps a factor in the poor response to the preoperative management of her hyperthyroidism.

Case 2. Mrs. S. T., a 69-year-old widow, was admitted to the Evans Memorial on October 13, 1937, complaining of extreme nervousness and rapid onset of the cardinal symptoms of hyperthyroidism during the previous 3 weeks. She had lost 15 pounds during this time, a total of 43 pounds in a year. For 3 weeks, there had been marked palpitation, dyspnea and weakness. There was no ankle edema or chest pain.

Examination revealed an undernourished woman who was nervous and worried, and showed mild activation. The skin was warm and moist. There was no exophthalmos. There was a fine tremor of the extended tongue and fingers. The thyroid gland was symmetrically enlarged to one and a half times the normal size. In addition, a coincidental, discrete 2.5-cm. adenoma was palpated in the right lobe. The heart was slightly enlarged, and the rhythm was regular. However, on the day following admission, paroxysmal auricular fibrillation was noted, and this continued throughout the preoperative course. The blood pressure was 140/78.

The basal metabolic rate was +35 per cent. A photometer reading showed a moderate deficiency in vitamin A. The patient was put on large doses of vitamin A for 15 days, without any real effect on the metabolism, but with marked improvement of the photometer reading. She was then given Lugol's solution, 10 minims three times a day, beginning on the 19th day. On the 36th day, the basal metabolic rate had fallen to −2 per cent (after 17 days' treatment with Lugol's solution). The patient was transferred to the Thyroid Service on the 38th day after admission, when slow auricular fibrillation and moderate cyanosis were evident. She was seen by the cardiologist, Dr. Ashton Graybiel, who considered the cardiac reserve adequate and believed that the patient should be fully digitalized preoperatively. This was done during the next 16 hours.

A first-stage hemithyroidectomy was carried out on November 23, 1937, under cyclopropane and oxygen anesthesia. The patient's condition was satisfactory during the initial stages, and she continued to fibrillate at a slow rate, 50 to 80 beats per minute. The blood pressure, which was 136/94 the day before operation, rose to 184/84 at the beginning of anesthesia and to 214/140 after 10 minutes; the pulse rose to 116. After 14 minutes of operating time, the patient suddenly stopped breathing and became pulseless. In spite of artificial respiration, she could not be revived and died before completion of the operation.

Post-mortem examination revealed no gross, obvious cause of death. The thyroid gland was diffusely hyperplastic. The lungs were essentially normal. The heart showed slight dilatation, and the myocardium was notably soft and flabby. The coronary arteries were sclerosed, with marked fibrous thickening of the intima, in places amounting to almost complete occlusion. Acute cardiac decompensation and acute dilatation of the heart were regarded as the causes of death

The patient was obviously a very serious risk. She was sixty-nine years old and had lost a large amount of weight (43 pounds) over a period of one year. Latent hyperthyroidism had probably been present for a much longer period than the three weeks of obvious hyperthyroidism. Limited cardiac reserve and actual cardiac damage were present, as shown by auricular fibrillation, dyspnea and palpitation. In retrospect, three questions arise. Would some other anesthetic have been less severe on the patient, would a more conservative operation in the form of pole ligation have been preferable, or should we have taken much longer in our preoperative preparation? In the great majority of serious-risk patients, it is our opinion that the operation can be brought to a speedier conclusion, with less trauma to the patient, under general anesthesia in the form of cyclopropane and oxygen administered by an experienced physician anesthetist. Perhaps, initial ligation of the superior thyroid vessels, first on one side and then on the other, followed by a two-stage hemithyroidectomy, would have helped this patient. In the light of our past experience, single-pole ligation has often failed to arrest the progress of the disease, because of the marked collateral vascularity of the thyroid gland. Consequently, we have placed greater reliance on adequate, rigidly careful preparation of the serious-risk patient for a quick hemithyroidectomy. Actually, this has given us greater assurance in arresting and controlling the hyperthyroidism. The questions of whether this patient could have survived four planned, graded, operative procedures or should have had longer preoperative care cannot be answered.

Case 3. W. M., a 53-year-old dyer, was admitted to the hospital on November 3, 1938, complaining of increased irritability, nervousness and a loss of 34 pounds in 1 year. Symptoms including crying spells were severe for 3 months, and iodine (5 drops three times a day) had been taken for 12 months before admission. Dyspnea, orthopnea and ankle swelling had been noted for 2 weeks. One brother had died of "goiter" at the age of 34 years.

Examination revealed an 118-pound man who was activated, mentally confused, indifferently co-operative and unreliable in history. There was exophthalmos of the right eye only. The thyroid gland was firm and symmetrically enlarged to three times the normal size. There was no heart disease.

The basal metabolic rate was +53 per cent on admission, and 14 days later +16 per cent. However, the patient lost 5 additional pounds during that period.

Sixteen days after admission, a right hemithyroidectomy was performed, without incident. The course was uneventful for 24 hours, when a temperature of 103°F. and auricular fibrillation at the rate of 130 beats per minute developed. The patient responded well to intensive supportive

therapy until the afternoon of the 2nd day, when his temperature rose to 106°F. Ice packs and sodium amytal by rectum produced temporary improvement, without evidence of cardiac failure. However, the patient died suddenly that night, 61 hours after operation, of uncontrolled thyroid crisis. Autopsy revealed bronchopneumonia and pulmonary edema, but no other cause of death.

*Adenomatous Goiter with Hyperthyroidism*

Forty-seven operations were performed on 40 patients, with 2 deaths, giving an operative mortality of 4.3 per cent. The youngest patient was twenty-five years and the oldest seventy years of age. Twenty-nine patients were over and 11 under forty years. There were 36 females and 4 males, a ratio of 9:1. Many of these patients had had asymptomatic goiter for years, the longest duration being forty years. Relief was sought only when complications, especially hyperthyroidism, appeared. Thyroidectomy was performed in two stages on 7 patients, or 18 per cent of the cases.

Pathological examination disclosed areas of secondary hyperplasia in the multiple colloid adenomatous goiter in 26 cases. In the remaining 14 cases, multiple colloid adenomatous goiter was reported, with associated fetal or embryonal adenomas in 3 cases, secondary hemorrhages in 3, and associated simple adenomas in 4. These 14 patients were considered to have so much clinical evidence of hyperthyroidism that they were so classified, even though the pathological examination did not disclose substantiating hyperplasia.

There were 9 thyrocardiac patients, and 1 death occurred in this group. Another patient developed postoperative thyroid crisis, terminating in death after forty hours. Two patients recovered from impending crisis. Three patients had transient auricular fibrillation postoperatively.

Four hours after operation, the one postoperative hemorrhage of the entire series occurred in this group. Secondary operation for control of the hemorrhage was followed by uneventful recovery. One patient had transient immobility of the left vocal cord that cleared in two months. One patient sustained permanent injury to the left vocal cord, which was present thirty-seven months later. There was no case of bilateral nerve injury in the entire series. No patients were known to have developed recurrent hyperthyroidism, hypothyroidism, myxedema or hypoparathyroidism.

The 2 fatal cases are reviewed below.

Case 4. G. G., a 67-year-old man, was admitted to the hospital on November 25, 1936, with a swelling of the neck that had been present since childhood and had shown gradual growth in the preceding 12 years. For 6 months, increased warmth, marked tremor of the hands and extreme weakness had developed, with no loss of weight. The neck had become smaller, that is, a size-20 collar became too large, suggesting descent of the goiter into the upper mediastinum.

Examination revealed a 168-pound, well-preserved man showing definite activation, with tremor of the extended tongue and fingers. The thyroid gland on the left was replaced by a nodular mass five times the size of the normal lobe; the right lobe was smaller but enlarged. The trachea was deviated to the right, with moderate compression. The heart showed no gross enlargement. The pulse rate was 100.

The basal metabolic rate was +31 per cent, and 11 days later, it was +19 per cent. Two days before operation, the pulse rate rose to 148, and auricular fibrillation developed. The patient was digitalized, 15 gr. being given over the 2-day period before operation.

A first-stage hemithyroidectomy was done 3 weeks after admission. The next day, the patient's condition was considered very satisfactory, with the pulse regular at 70 beats per minute, and the temperature 100.6°F. That afternoon, 90 minutes after an intravenous infusion of 750 cc. of 10 per cent glucose and Lugol's solution, 10 minims in physiologic saline solution, the patient developed a chill, became cyanotic and fibrillated. Respirations rose to 35 per minute. Despite oxygen and uninterrupted digitalis therapy, the temperature rose steadily to 104°F. by axilla, and the patient became semicomatose; pulmonary congestion developed, without edema. He died 40 hours after operation.

The cause of death was regarded as postoperative thyroid crisis leading to failure of first the pulmonary and then the general circulation. No definite opinion could be formed concerning the possible precipitating effect of the intravenous infusion. Autopsy revealed no significant local changes and substantiated the clinical impression of the cause of death.

A review of the preoperative management of this patient brings to the fore the sudden development of auricular fibrillation for the first time two days before operation. This certainly gave a further warning of the serious risk involved in this patient. A longer period of digitalization and cardiac therapy might have averted the fatal outcome. From this and other experiences, we believe that when digitalization is carried out, a delay of several days in operation should follow.

Case 5. Mrs. A. S., a 61-year-old woman, was admitted to the hospital on November 26, 1941, with goiter for 20 years and symptoms of hyperthyroidism for 8 months. Lugol's solution, 15 minims daily for 6 months, had been attended by temporary improvement, followed by progressively severe hyperthyroidism. The patient had lost 15 pounds in the previous year.

Examination revealed a thin, activated elderly woman in the "iodine-fast" state of hyperthyroidism. The thyroid gland was nodular and enlarged to four times the normal size on the right, and slightly less on the left.

The basal metabolic rate was +48 per cent, and 8 days later was +46 per cent. The pulse rate ranged from 76 to 128, and on the morning of operation was 76.

Fifteen days after admission, a right hemithyroidectomy was done without difficulty. Six hours later, the temperature rose to 105°F., and the classic picture of thyroid crisis developed. On the 2nd postoperative day, auricular premature systoles were disclosed by electrocardiogram. The pulse rose to 200 per minute, and the temperature

ranged from 103 to 105°F.; coma and death occurred on the 3rd postoperative day.

The cause of death was uncontrolled hyperthyroidism; post-mortem examination disclosed no other cause.

*Recurrent Hyperthyroidism*

Twenty operations were performed on 18 patients who had had previous operations for hyperthyroidism. There were no deaths. Five patients were considered to have persistent hyperthyroidism following operation within the previous two years. The remaining 13 patients had been free from symptoms for from two to twelve years; these were regarded as patients with recurrent rather than persistent hyperthyroidism. All patients appearing for secondary operations for the control of hyperthyroidism have been grouped under the single term "recurrent," however, for the management of both the persistent and truly recurrent cases is identical.

Sixteen patients originally had diffuse goiter of the exophthalmic type, confirmed pathologically as primary hyperplasia of the recurrent remnant. Only 2 showed recurrent nodular goiter with secondary hyperplasia of the remnants.

Fifteen patients had a one-stage reoperation. Two had divided reoperations at six-week intervals. One patient required two reoperations, twelve and thirty months, respectively, after the original thyroidectomy for exophthalmic goiter. There were 3 thyrocardiac patients, in all of whom only single-stage reoperation was necessary.

Preoperative examination of the vocal cords, although desirable in all patients undergoing thyroidectomy, is especially so in those on whom reoperation is contemplated. One patient had paralysis of the left vocal cord following thyroidectomy thirty-seven months previously. Such information aids greatly in averting possible further damage and bilateral vocal-cord paralysis.

None of these patients developed postoperative hemorrhage, thyroid crisis or recurrent-laryngeal-nerve injury. One patient, who developed clinical tetany from hypoparathyroidism on the fourth postoperative day, had had two operations for exophthalmic goiter, eight and seven years previously. Two months after the onset of mild tetany, she was adequately controlled on a regime of calcium and dihydrotachysterol (AT 10), but continued therapy was necessary. One patient developed hypothyroidism and myxedema a year after operation.

NODULAR GOITER WITHOUT HYPERTHYROIDISM

All 74 patients in this group were subjected to single-stage thyroidectomy, and there were no fatalities. Many of the goiters were described as subclavicular and substernal in position, and several as intrathoracic. However, none were so truly intrathoracic as to require splitting of the sternum or to cause undue technical difficulty of removal through the usual thyroidectomy approach.

The distribution of the pathologic types encountered is presented in Table 3. Much emphasis has been laid on the parenchymatous, embryonal or fetal adenoma as representing a true tumor type, in contrast to the colloid or simple adenoma. The parenchymatous adenoma was found in only 4 patients, and the colloid adenoma in 36 — nine times more frequently.

TABLE 3. *Summary of Cases of Nodular Goiter without Hyperthyroidism.*

| YEAR | TOTAL NO. OF CASES | DIAGNOSES | | |
|---|---|---|---|---|
| | | MULTIPLE COLLOID ADENOMATOUS GOITER | SIMPLE ADENOMA | FETAL ADENOMA |
| 1936 | 3 | 1 | 2 | 0 |
| 1937 | 12 | 6 | 6 | 0 |
| 1938 | 16 | 5 | 9 | 2 |
| 1939 | 16 | 9 | 6 | 1 |
| 1940 | 9 | 5 | 3 | 1 |
| 1941 | 18 | 8 | 10 | 0 |
| Totals | 74 | 34 | 36 | 4 |

The postoperative complications were limited to one permanent and one transient unilateral recurrent-laryngeal-nerve injury that cleared in ten weeks. One patient developed coincidental catarrhal jaundice on the third postoperative day. No deaths occurred.

CARCINOMA OF THYROID GLAND

Seven patients with thyroid carcinomas were operated on during this six-year period. In 5 cases, radical thyroidectomy was carried out, but in none were the cervical lymph nodes or internal jugular vein removed. The remaining 2 patients were subjected to biopsy only, and 1 of these died of myocardial failure on the eighth postoperative day. The surviving 6 patients received postoperative x-ray treatment.

A fifty-one-year-old patient who showed clinical hyperthyroidism associated with unsuspected carcinoma had had symptoms of hyperthyroidism for eight months, with a loss of 12 pounds and an initial metabolic rate of +50 per cent. A subtotal thyroidectomy was done for exophthalmic goiter. However, pathological examination revealed papillary adenocarcinoma in one portion of the diffuse primary hyperplasia seen throughout. The metabolism was -6 per cent seven days later. Examination twenty-six months later revealed the patient to be symptom free, with no signs of recurrence.

Except for the 1 fatality, which is reviewed below, there were no complications. The 6 sur-

viving patients have remained symptom free for four to twenty-six months after operation.

Case 6. Mrs. A. A., a 71-year-old housewife, was admitted to the hospital on February 4, 1938, having noted swelling of the left side of the neck for 6 weeks. She had lost 35 pounds and had noted hoarseness for 3 weeks. The swelling grew constantly larger and more painful during this short period.

Examination revealed a well-preserved woman with normal findings except for hoarseness and the swelling of the neck. The left lobe of the thyroid gland was enlarged to four times the normal size; the mass was hard and fixed, and involved the isthmus. The right lobe was not palpably enlarged. There were several hard, cervical lymph nodes, 1 cm. in diameter, on the right. The trachea was displaced to the right. General arteriosclerosis was evident.

Biopsy of the thyroid gland was performed 10 days after admission. The pathologist reported a rapidly growing, exceedingly anaplastic, embryonal tumor, probably of thyroid origin. From the 2nd postoperative day, the patient developed progressive signs of myocardial failure, and succumbed on the 8th day after operation. No autopsy was performed.

The problem of managing the patient with a solitary thyrogenic metastasis of the skull has arisen once in this series. Active intervention, with removal of the long-standing calcified malignant adenoma of the right thyroid lobe, followed by craniotomy and removal of the skull metastasis, was carried out. No further recurrence had appeared twelve months after operation.

### Rarer Conditions

Three patients were seen with parathyroid adenoma, profoundly altered calcium metabolism and bone changes. One was moribund on admission. Excision was carried out on the remaining 2 cases. One patient survived and made a striking, sustained recovery. These records are being prepared for publication.

The congenital anomalies were few in this series. Lateral aberrant thyroid tissue was removed from the neck in 2 cases. Persisting remnants of the thyroglossal duct were also removed from 2 patients. No patients with lingual thyroid tissue were seen. No complications and no deaths occurred in this group.

### Summary

A six-year review of the Thyroid Service at the Massachusetts Memorial Hospitals is presented. Since this is a general ward service, many of the seriously ill patients first appeared in advanced, untreated stages of thyroid disease. They showed evidences of dietary deficiencies and constitutional disease. In the treatment of such patients, our experience has justified, we believe, the relatively high rate of divided operations (31 per cent) in the 197 patients with hyperthyroidism. In spite of this conservative approach, a thyroid crisis developed in 16 of these 197 patients, 4 of whom died. It is apparent that in a ward thyroid service, therefore, one must take a longer time and give more detailed care in the preoperative preparation of patients with hyperthyroidism if the same low mortality figure as that among private patients is to be obtained.

The morbidity and mortality rates have been constantly kept before us in our efforts to improve these results. Although the mortality rate of 1.7 per cent among patients with exophthalmic goiter conforms with results generally obtained, it is interesting that no patient died of this disease during the last three years.

The patients having adenomatous goiter with hyperthyroidism showed a mortality of 4.3 per cent. There were 2 deaths in the 40 cases, both due to thyroid crisis. Associated cardiovascular impairment was present in 23 per cent of these cases, whereas only 13 per cent of the exophthalmic group showed this complication. These patients were on the average much older than the exophthalmic patients, and the goiter was of long standing.

There was no mortality in the eighteen secondary operations for recurrent toxicity.

The four permanent, unilateral recurrent-laryngeal-nerve injuries represent a rate of 1.2 per cent in three hundred and thirty-four thyroid operations. An additional 3 patients, 0.9 per cent, sustained temporary nerve injury such as may result from undue traction, crushing or hemorrhage into the nerve area, with demonstrated recovery of function in two to twenty-eight weeks. Postoperative hypothyroidism and myxedema were noted in 12 of 288 patients, a rate of 4.2 per cent. This complication is far preferable to persisting toxicity and, in certain thyrocardiac patients, is even desirable. If necessary, it is readily treated.

The long-continued use of iodine in the unoperated patient with hyperthyroidism was discouragingly frequent. These patients were more difficult to prepare for surgery, the operative risk was greater, the postoperative reaction was less amenable to control, and a fatal outcome was more frequent. Three patients, or 60 per cent of those who died in the hyperthyroid group, had been given daily iodine for from one to six months before surgery was advised and carried out.

Experience has led us strongly to advise against the use of iodine in these patients until active plans for surgical treatment have been made by the physician and agreed to by the patient. Attempts to control hyperthyroidism with nonsurgical measures not only delay unjustifiably, we believe, ef-

fective control of the disease, but increase the likelihood of complications before and after thyroidectomy and thereby lessen the usual safety of the procedure. The iodine-fast patient with hyperthyroidism should disappear as soon as physicians are ready to accept the facts that surgery is a safe and rapid method for curing hyperthyroidism and that, in outspoken thyroid toxicity, iodine does not produce a cure.

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# THE PHYSICIAN PREPARES TO ENTER THE ARMY

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THE proposed increase in the size of the Army of the United States indicates that many physicians will find themselves in the armed services in the near future. The average physician is so busy with everyday practice that he has little time to think about the multiple preparations necessary before he enters the service. Many questions arise regarding how to proceed to close the office, provide for dependents and prepare for entrance into the Army. Having experienced these problems and answered many inquiries, we offer the following suggestions. Although many of these suggestions are obvious and others may be outdated or changed radically before this article is published, some of them may be helpful.

## CLOSING OFFICE

One should take an inventory of all instruments, equipment and furniture and evaluate these articles in case it becomes necessary to sell them or to collect insurance for fire or theft.

One should arrange for storage of equipment and see that it is fully covered by insurance, unless it is to be used by another physician.

All narcotics should be locked up or returned for credit; it is not necessary to renew the narcotic license.

All case histories, especially cases in which litigation may be involved, should be completed. A physician who is entering the service should instruct his representative or attorney in the use of his files and their contents.

Accounts payable and receivable should be audited and explained in detail to the representative or attorney. A note should be appended to statements rendered for professional services informing patients that one is called to active duty, since this appeal often brings results.

Office subscriptions to popular magazines should be canceled. It is usually wise to continue professional journals, with a change of address, until one is certain that they are available in hospital libraries of future stations.

Arrangements to cancel or adjust rent or sublet office space should be made. If the renewal of the lease for office space is due in the near future, and there is a possibility of one's being called to active duty, this renewal should contain an army clause to become effective on the date of call to service.

Service for gas, electric light, telephone, laundry and so forth, should be canceled.

Employees should be provided with a letter of recommendation.

Since service in the Army does not release one from the danger of malpractice suits, it is wise to maintain professional protective insurance. However, the validity of such insurance, while one is on duty, especially on foreign soil, should be checked — some companies are issuing a special low-cost policy covering malpractice insurance in military service. The insurance company should be notified of entrance into the service and change of address.

All medical societies of which one is a member should be notified of the date of call to service. Many societies will keep the names of those entering the armed forces on their inactive list until they return, without financial obligation.

It is advisable to take along any instrument, such as an ophthalmoscope or stethoscope, that one has become accustomed to using with ease and without which one may be handicapped.

A request for leave of absence should be written to the secretary of the staff of the hospitals and medical school where appointments are held, or with which one has been affiliated.

It is a matter of personal opinion of how best to notify patients of entrance into the services. This may be done by personal calls, printed announcements or form letters. If one's practice has been assumed by another physician, this fact may also be announced by the above methods.

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### Providing for Dependents

The chief concern of most physicians will be providing for the family. Budgets must be readjusted to the new fixed income (Table 1). It is wise to plan this readjustment early, so that all changes will be gradual and all eventualities may be foreseen.

It is unwise to plan on moving the family until it can be determined when one will be called and where the first permanent station will be located. The first station may be near one's present home.

Taking the family is unsatisfactory, since adequate living quarters near army camps are difficult to find, rents are invariably high and there will be frequent and unpredictable changes of station.

It is essential to consult a competent lawyer in planning and settling one's business affairs.

A last will and testament should be made, regardless of dependents.

A power of attorney should be granted the wife or another trustworthy and competent person, so that one's business may be managed properly. A limited power of attorney may be given a secretary, who is familiar with the accounts payable and receivable that will continue for a time after the office is closed.

All documents, such as deeds, wills, insurance policies, copies of power of attorney and birth certificates, should be stored in a safety deposit box accessible to the wife and attorney.*

### Army Pay and Allotment

For the first time, the majority of physicians will receive a relatively fixed salary, varying only with rank, length of service and special compensation for service overseas. This salary, which is paid once a month in cash or by check, may be deposited by the local finance officer in the bank of one's choice. Each officer receives a 5 per cent increase in base salary when he completes three years of active duty, six years of inactive duty or any equivalent combination of service. This is known as a "fogey." A 10 per cent increase in base pay is provided when an officer serves overseas. Single officers, living in adequate quarters provided by the Government, are not given a rental allowance. While one is on duty in the United States, allotments of pay can be made only for payment of governmental or commercial life-insurance premiums. On duty outside the continental limits of the United States or in Alaska, one can allot any or all of the base pay, longevity and ration allowance to any bank or insurance company. These amounts can be calculated from Table 1.

Table 1. *Approximate Pay of Medical Officers.*

| Fraction | First Lieutenant | | Captain | | Major | | Lieutenant Colonel | |
|---|---|---|---|---|---|---|---|---|
| | Married | Single | Married | Single | Married | Single | Married | Single |
| Base pay | 166.67 | 166.67 | 200.00 | 200.00 | 250.00 | 250.00 | 291.67 | 291.67 |
| Rental allowance | 60.00 | 40.00 | 80.00 | 60.00 | 100.00 | 60.00 | 120.00 | 80.00 |
| Ration allowance | 36.00 | 18.00 | 36.00 | 18.00 | 54.00 | 18.00 | 54.00 | 18.00 |
| Totals | 262.67 | 224.67 | 316.00 | 278.00 | 404.00 | 328.00 | 465.67 | 389.67 |

Single officers with dependents may receive married officers' salaries if the dependency is adequately proved by certification and affidavits.

### Insurance

Since many physicians have major investments in insurance, this subject deserves special consideration.

The validity of all insurance policies while one is in service should be reviewed. Most policies issued during the latter half of 1941 contain a war clause. The clauses that govern the continuation of policies in the event that one is unable to pay the premiums should be clarified. Such problems can be discussed with any competent insurance broker or a qualified representative of the insurance company. There are no set rules for insurance, since each policy is an individual contract, and policies vary with the company and the type of coverage. Although no set directives can be given, the following suggestions may prove of benefit.

A résumé of all insurance policies, listing the name of the insurance company, type of insurance, amount of policy, amount of premium and date on which the premium is due, should be prepared. Copies should be furnished to the persons designated to manage the affairs of the physician who enters the service.

A permanent mailing address (not an army address) should be established in one's name in care of the wife or attorney, so that premium notices will be received and paid promptly.

In general, policies lapse in thirty-one days if the premiums are not paid. A statement of health must be submitted in the following thirty-day period, or policies are finally dropped. Absence without proper safeguards and the impossibility of quick communication invite this danger. If ninety

*LaGarde, R. D. Concerning dependents. *Coast Artillery J.* 85:14 (Mar.-Apr.), 1942.

days have elapsed, the policy may then be considered void, and the company may refuse to reinstate the policy on payment of back premiums or may reinstate the policy with a war clause inserted.

It is possible to pay up policies for more than a year in advance by a single cash payment. Interest usually accrues at bank rates, and any excess is refunded if the policy is terminated.

Information should be obtained regarding what happens to each policy if one is unable to pay the premiums from current income.

The better plan is that incorporated in an "automatic premium loan clause." This permits the use of the cash value of the policy for payment of future premiums. If not already included, this clause should be written into the contract. If it is planned to use this method of payment, written authorization must be given to the company. This is not applicable to term insurance, which has no loan value.

If the company will not grant the automatic premium loan option, the policy is governed by the so-called "nonforfeiture option." This option provides the choice of accepting a reduced amount of paid-up or extended insurance at its full value until the cash value of the policy is used up. This selection seems desirable in providing full protection during service in the Army.

Double indemnity is usually not paid in war except for fatal accidents common to civilian life. The disability clause does not hold during military service. Some companies will refund this portion of the premium on a pro-rata basis. Likewise, some companies will reinstate the disability clause after return to civil life if a medical examination is passed.

Is the policy invalidated by airplane travel? If not, is there any limitation concerning the type of carrier and number of flights. In many policies, double indemnity is not paid except in fatal accidents occurring on regular fare-paying passenger lines. Double indemnity would not be paid for accidents occurring in the Army Air Corps.

Term insurance especially must be analyzed. If it is necessary to convert it while one is in service, one should make certain that the war clause is not inserted. One must provide the additional money necessary for conversion back to the date of purchase, to avoid insertion of the war clause. If term insurance is converted gradually, the dates of conversion and amount of increase of premium must be carefully explained to those responsible for paying the insurance premium. An immediate conversion to ordinary life insurance is advisable if financially possible.

To avoid nonpayment of premium, it is possible, if on duty outside continental United States or in Alaska, to have the Government pay premiums directly to the insurance company and make the necessary deduction from base pay. This is called "payment by allotment." It will be necessary to adjust the premium to a monthly payment plan, for annual and quarterly payments are not possible by allotment.

Government insurance is available up to $10,000. This cheap and highly desirable insurance may be obtained by consultation with the adjutant of the organization. It is not available until after induction into the service. Although it is initially term insurance, it may be converted after a year and before five years have elapsed. The monthly premiums vary from $7.10 at thirty years of age to $8.50 at forty.

The advisability of continuing health and accident insurance policies should be considered, since the benefits from these policies are limited while the physician is in the armed services. Most policies are good only for conditions common to civilian life in the United States. Noncancelable policies merit special consideration, for they may be impossible to obtain when one returns to civilian life.

All other types of insurance should be renewed, and one should be certain that coverage is complete for fire, theft, liability and so forth on car, household goods and real estate. Adequate preparation for payment of such premiums, many of which fall due every three years, should be made.

All policies should be stored in a safety deposit box.

It is wise to provide the wife or attorney with a copy of marriage certificate and birth certificates of oneself, wife and dependents so that relationship may easily be proved if it becomes necessary to collect pensions or insurance. These documents should be placed in a safety deposit box.

### Taxes and Mortgages

Service in the Army does not excuse one from payment of taxes. Although the Soldiers and Sailors Civil Relief Act of 1940 permits deferment of payment of federal taxes by members of the armed forces, this deferment is not automatic. Inability to pay taxes from current income must be proved by the submission of a sworn statement of financial condition at the time the tax return is filed. The attorney should be provided with a list of taxes payable and the dates on which they are due, and with all information necessary to file income-tax returns on income from practice and investments. Arrangements should be made for

payment or readjustment of any mortgages that may be held. Army salaries are subject to the state and federal income taxes.

Although the Relief Act of 1940 provides protection for men in the service on certain other classes of debt in and prior to the passage of the act, one should consult a competent attorney in any specific case in which relief is desired.

### Uniform

It is customary to report for active duty in uniform. It is, of course, a great temptation to buy an extensive wardrobe. It cannot be overemphasized that one should purchase only a minimum of clothing. Great savings and better selection can be effected if one purchases most articles from the post exchange and quartermaster after reporting for duty.

The prescribed uniform varies with the type of assignment and with the climate. A safe minimum purchase providing a standard dress uniform regardless of the location of station or time of year is as follows:

1 overseas cap.
1 woolen blouse with cloth belt (Sam Browne belts are no longer required).
1 pair of woolen trousers (either "pink" or to match blouse).
1 cotton shirt.
1 woolen shirt (field).
1 web belt (plain buckle).
2 pairs of solid-color tan or brown socks.
White or tan handkerchiefs.
1 necktie of new M-3 shade (black ties are no longer worn).
1 overcoat (if possible, one should not buy an overcoat until arrival at post; if weather is inclement, a gabardine raincoat may be worn).
1 complete set of insignia (one should refer to *Officer's Guide* for correct placement on uniform).
All solid tan and brown shoes are acceptable. (It is not considered necessary to wear any special military shoe unless one is ordered to do so. One should remember that there is much walking and marching during the initial period of training on active duty, and should provide oneself with a pair of comfortable, waterproof, well-broken-in high shoes.)

Every article of clothing should be marked with one's name. Rank and name of organization should be omitted. Linen or rayon tape, embroidered or stenciled with indelible ink, is most frequently used. A timesaving device is a rubber name stamp with an indelible ink pad for stenciling flat pieces, such as handkerchiefs, sheets and towels.

All personal effects should be stored, and all woolen clothing should be cleaned and made mothproof before storage.

Useful reference books that may be purchased are: *Officer's Guide* (seventh edition—February, 1942), *Military Medical Manual* and *Handbook of the Medical Soldier.*

The following luxuries will add much to one's comfort and enjoyment during camp life but are not essential: radio, camera, electric razor, spot-type bed lamp, small bedside floor rug and so forth.

The change from civilian to army life is radical, and yet the readjustment is rapid, and many a busy physician will appreciate the change. Incidentally, he may be called on to assume the responsibility of doing his own laundry. If so, all woolens should be treated with due respect and washed carefully in lukewarm water. Many a new officer has been horrified by the atrophy of his beautiful hand-knit socks following his first effort at the wash tub.

# EXPERIMENTAL APPLICATION OF SULFONAMIDE DRUGS TO THE CEREBRAL CORTEX*

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BECAUSE of war conditions, widespread use of the sulfonamide drugs in wounds of all parts of the body has developed. The obvious effectiveness of these chemicals in helping to minimize infections[1] has resulted in their clinical employment with very little experimental basis, whereas ordinarily there would be ample opportunity for thorough laboratory trial. This has been particularly true in craniocerebral injuries, in which the opportunity for clinical trial has been all too readily available.

It is apparent that experimental control of this type of chemotherapy,—that is, direct application to the brain and meninges,—is being undertaken in many laboratories, and some surgeons have had an opportunity to see even late effects of such application in patients. To date, extraordinarily little accurate information has been published or otherwise made available to the interested medical public. Several extensive projects are now under way, and it is probably just as well that these be made by several observers, since important discrepancies in results have already been reported. Pilcher and his associates,[2] who are carrying on an investigation of the chemotherapy of intracranial infections, were so impressed by the harmful effects of the use of sulfathiazole that they published a preliminary report on the convulsions produced by intracranial implantation of sulfathiazole. Almost concurrently with their report, Penfield,[3] following a trip to Great Britain, refers to the fact that some British neurosurgeons have been so favorably impressed by the effect of local application of sulfathiazole that they have taken to placing it routinely within all craniotomy incisions before closure. It seems obvious that the experimental phase of this problem lags considerably behind the clinical. Probably the most complete and most valuable work reported so far, from the Montreal Neurological Institute, was summarized recently by Hurteau.[4]

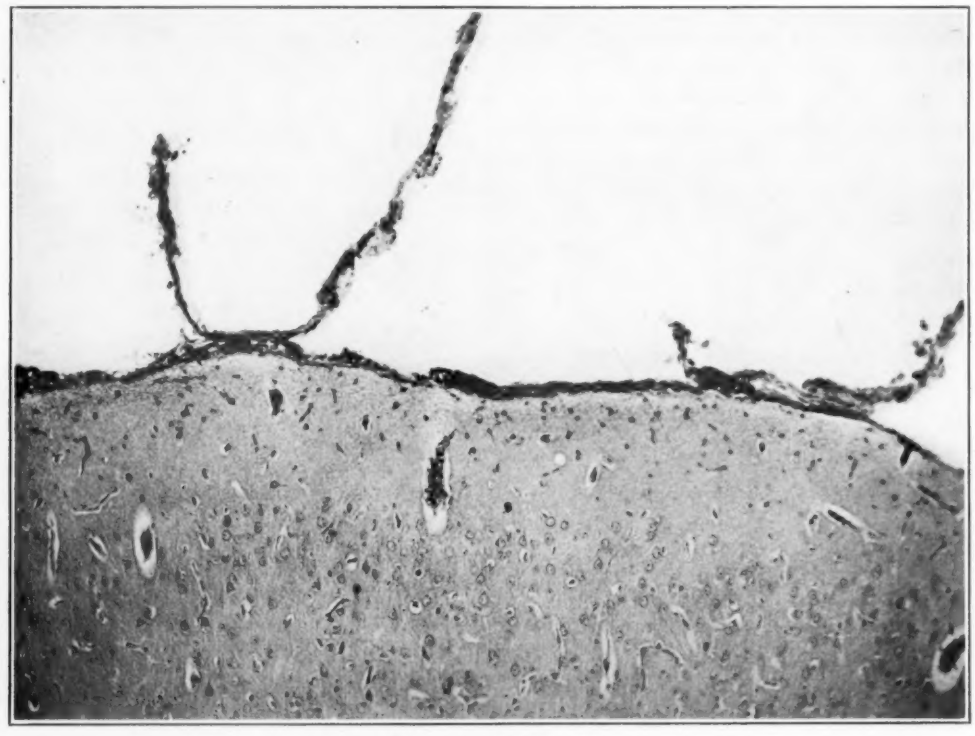

FIGURE 1. *Cat No. 1.*

*Photograph of a section of the cortex of a cat in which operation had been performed under nonsterile conditions but with sulfanilamide added (× 125).*

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Undoubtedly, other complete studies will be reported in the near future.

In the hope that some unnecessary duplication of effort may be avoided, these somewhat simpler preliminary experiments are recorded. Sulfanilamide, sulfathiazole and sulfadiazine were applied to the cortex of cats under sterile and unsterile conditions, and since we were most interested in the use of sulfadiazine, this drug was applied to the surface of the brains of three monkeys.

The cat experiments were carried out as follows. With full aseptic surgical technic, a midline incision was made, the temporal muscles incised, and a trephine opening 1.5 cm. in diameter made in the parietal bone on both sides. The dura was opened on both sides, and on one side, the pia-arachnoid was torn and the cortex was traumatized very superficially with a sharp needle. In the control animal, no drug was used. The sulfonamide drugs, in powder form, were applied to the cortex of both sides and to the superficial tissues. Five tenths of a gram of powder was used in each case, a definite layer completely covering the exposed brain being obtained. In a second group of animals, the same operation was then carried out, and drugs were applied under nonsterile conditions: the instruments used were clean but not sterilized, the animals were not shaved, and no cleansing agent was applied to the skin. The results of these experiments are shown most clearly in Table 1 and Figures 1 and 2.

TABLE 1. *Summary of Cat Experiments.*

| Cat No. | Drug Used | Postoperative Day Killed | Findings on Traumatized Side | Findings on Nontraumatized Side |
|---|---|---|---|---|
| Operation performed under sterile conditions | | | | |
| 86 | None | 14 | Normal | Normal |
| 87 | Sulfanilamide | 36 | Normal | Normal |
| 84 | Sulfathiazole | 7 | Normal | Normal |
| 20 | Sulfathiazole | 29 | Mild inflammation | Mild inflammation |
| 25 | Sulfadiazine | 23 | Normal | Normal |
| Operation performed under nonsterile conditions | | | | |
| 89 | None | 5 | Severe meningoencephalitis | Severe meningoencephalitis |
| 1 | Sulfanilamide | 29 | Dura adherent | Dura adherent |
| 2 | Sulfathiazole | 14 | Normal | Normal |
| 3 | Sulfadiazine | 26 | Normal | Normal |

In general, there was surprisingly little reaction to the drugs. One cat in which sulfathiazole was used died seven days after operation, and the cause of death was not clear. Other investigators[5] have reported that animals in which sulfathiazole was used have had convulsions and have died, presumably because of local irritation and absorption of the drug. In the animal in our experiment, no convulsions were observed, and the survival time seems long for death to have been due to absorption of the drug. When the experiment was repeated, the animal was sacrificed at the end of twenty-nine days, and a mild inflammatory reaction was found.

It is interesting that, except for the control animal that developed a severe meningoencephalitis, the cats subjected to operation under nonsterile conditions did extremely well. There was a slight inflammatory response to the drugs, but no actual infection, and when sulfadiazine was used there was no perceptible inflammation.

FIGURE 2. *Cat No. 89.*

*Photograph of a section of the cortex of a cat in which operation had been performed under nonsterile conditions and without a sulfonamide drug added (× 125).*

TABLE 2. *Summary of Monkey Experiments.*

| Monkey No. | Bone Flap | Drug Used | Postoperative Day Killed | Findings |
|---|---|---|---|---|
| 1 | Not replaced | Sulfadiazine | 54 | Adhesions of muscle, dura and cortex |
| 2 | Replaced | Sulfadiazine | 45 | Inflammatory reaction in dura |
| 3 | Replaced | Sulfadiazine | 45 | Normal |

Since sulfadiazine is probably the most effective of the three drugs in inhibiting the growth of a variety of organisms that would be likely to contaminate war wounds, we were most interested in its application to the cortices of three very large monkeys (*Macacus rhesus*). A bone flap was

turned down under sterile conditions, the dura opened widely, and 0.5 gm. of sulfadiazine powder spread over the cortex, dura, bone and superficial tissues. The experiments are summarized in Table 2. In one experiment, the bone flap was not replaced, and dense adhesions between muscle, dura and cortex resulted, as shown in Figure 3, taken when the animal was sacrificed at the end of fifty-four days. In the second experiment, there was a mild inflammatory reaction in the dura, and a collection of the powder was still grossly visible under the bone flap after forty-five days (Fig. 4). In this and the third experiment the dura stripped away from the arachnoid without any adhesions, and no drug was visible on the surface of the brain.

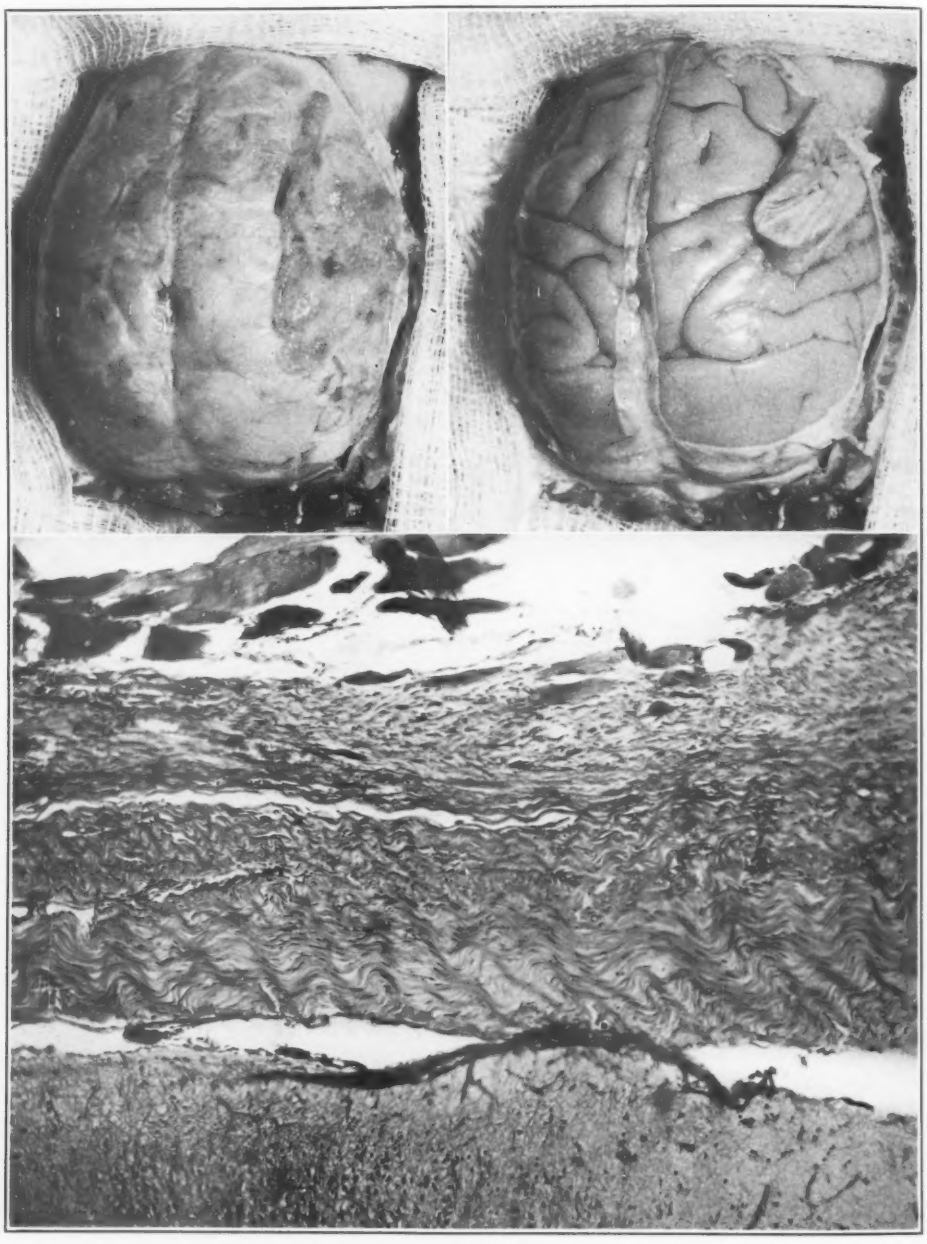

FIGURE 3. *Monkey No. 1.*

*This monkey was operated on with sterile precautions, the bone flap not being replaced; sulfadiazine was added. The upper photograph shows the gross appearance of the brain, before and after removal of the dura; the temporal muscle was adherent at the site of the flap. The lower photograph shows a section of the cerebral cortex at the site of the adhesion (× 125).*

Unfortunately, these monkeys were extremely difficult to handle, and it was possible to make postoperative blood and spinal-fluid determinations in only one. On this occasion, twenty-four hours postoperatively, the blood sulfadiazine level was 1.7 mg. per 100 cc., and the spinal-fluid level 1.0 mg. per 100 cc.

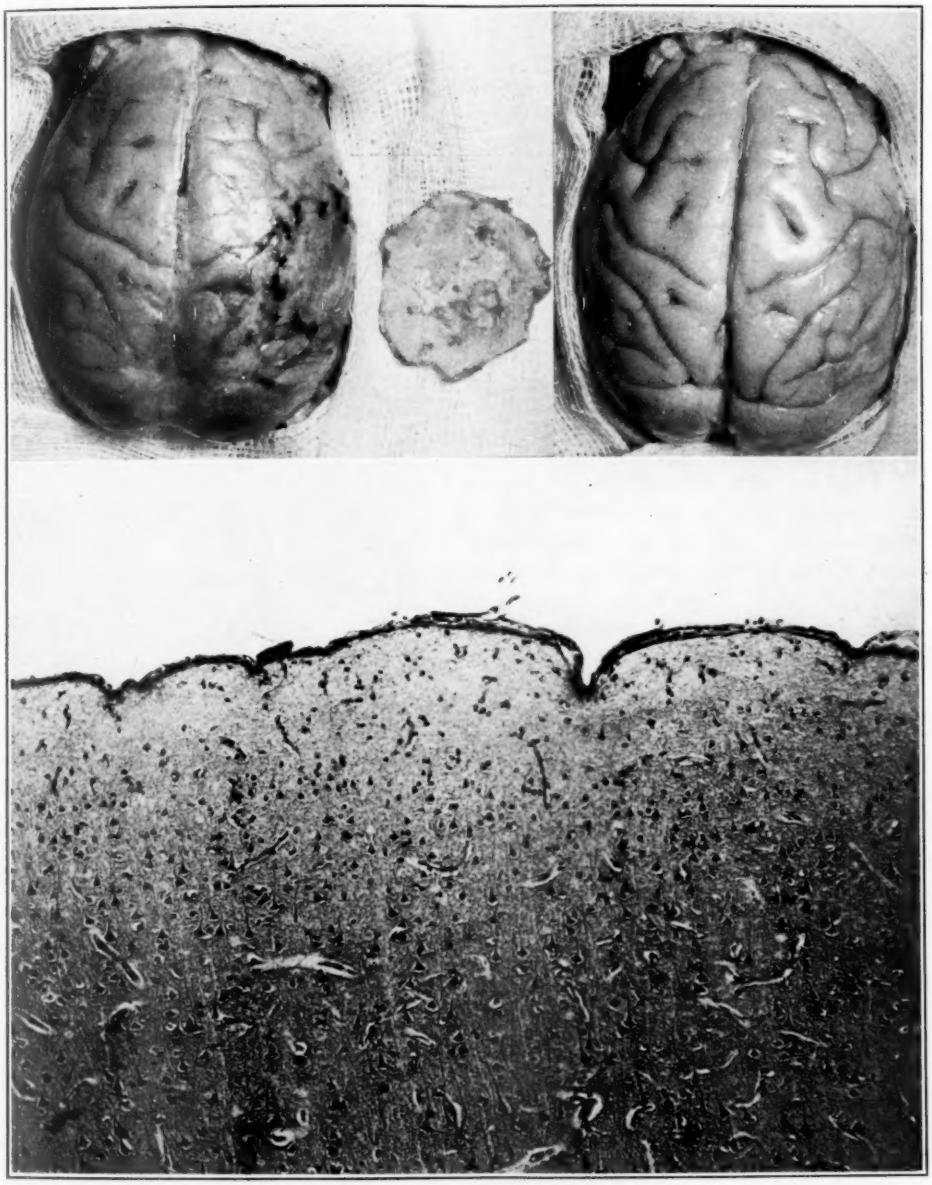

FIGURE 4. *Monkey No. 2.*

*This monkey was operated on with sterile precautions; sulfadiazine was added, and the bone flap replaced. The upper photograph shows the gross appearance of the brain, before and after removal of the dura and the inner surface of the bone flap, where some of the drug still remained. The lower photograph shows a section of the cerebral cortex (× 125).*

## SUMMARY

Sulfanilamide, sulfathiazole and sulfadiazine were applied directly to the cerebral cortex of 7 cats under sterile and nonsterile conditions. There was remarkably little inflammatory reaction except in the control cat under nonsterile conditions. Sulfadiazine was applied to the cerebral cortex of 3 monkeys. There was no perceptible inflammatory reaction, except in one, in which the bone flap was left out.

One may conclude that sulfadiazine powder, which is generally agreed to have a bacteriostatic action on the widest variety of organisms, can be safely used in the presence of gross contamination when the brain is not severely damaged. Further

work must be done to determine whether or not this conclusion can be applied to more complex craniocerebral injuries.


### References

1. Dingle, J. H., Thomas, L., and Morton, A. R. Treatment of meningococcic meningitis and meningococcemia with sulfadiazine. *J. A. M. A.* 116:2666-2668, 1941.
2. Pilcher, C., Angelucci, R., and Meacham, W. F. Convulsions produced by the intracranial implantation of sulfathiazole. *J. A. M. A.* 119:927, 1942.
3. Penfield, W. Clinical notes from a trip to Great Britain. *Arch. Neurol. & Psychiat.* 47:1030-1036, 1942.
4. Hurteau, E. F. The intracranial use of sulfadiazine: experimental study of the histology and rate of absorption. *Canad. M. A. J.* 46:15-17, 1942.
5. Watt, A. C., and Alexander, G. L. Epilepsy following application of sulphathiazole near the brain. *Lancet* 1:493-496, 1942.


## MEDICAL PROGRESS

# VIRUS PNEUMONIAS. II. PRIMARY ATYPICAL PNEUMONIAS OF UNKNOWN ETIOLOGY*


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DURING the last few years, there has been a great deal of interest in the increasing numbers of cases of acute respiratory infection associated with atypical pulmonary lesions in which the common pathogenic bacteria do not seem to play an etiologic role. The vast majority of the reported cases have occurred in adolescents and in young adults. Many of the reports have come from schools,[1-4] colleges[5-10] and army camps.[11, 12] Hospital personnel, particularly interns and nurses, have also featured prominently among the reported cases.[13-16] Although the mortality in these cases has been extremely low, the period of disability has been quite long. With the accelerated program of studies now in effect in most universities and with the rapid increase in the size of the Army, accompanied as it is by a shorter training period, these cases may constitute a significant problem from the point of view of "time out" from studies or the loss of man-days from training.

The name "virus pneumonia"[17-22] has been applied rather loosely to this group of cases and is probably the one most widely employed by practitioners. In most cases, the only justification for the use of this term is the failure to obtain pathogenic bacteria that can be considered etiologic. Individual authors have justified their use of the term on the basis of suggestive histologic findings in the pulmonary lesions,[17, 20, 22] or on the results of studies that suggested the presence of filterable agents.[14] Numerous other designations have been used in the description of similar cases. They include "acute influenzal pneumonia"[11]; "acute pneumonitis"[2, 3, 12]; "pneumonitis"[23, 24]; "acute interstitial pneumonitis"[7]; "atypical pneumonia with leukopenia"[8]; "current bronchopneumonia of unusual character and undetermined etiology"[15]; "bronchopneumonia of unknown etiology, Variety X"[16]; and "atypical bronchopneumonia of unknown etiology."[4] Most authors have believed that they were dealing with a specific infectious disease that constitutes a new entity.[7, 13] Reimann[13] suggested that it be called "acute infection of the respiratory tract, Type A" or perhaps "Type A virus pneumonia" if the virus etiology is confirmed,[13] or that the more general term "grip"[14] be used. Scadding[25] has attempted to classify certain more limited groups of cases according to the character of the pulmonary lesion, particularly according to their distinctive roentgenographic shadows, and has applied the name "disseminated focal pneumonia" to some of them; others he[26] called "benign circumscribed pneumonia." In a recent "official statement" to the Surgeon General of the Army prepared by the director of the Commission on Pneumonia, Board for the Investigation and Control of Influenza and Other Epidemic Diseases in the United States Army, it was suggested that, for purposes of classification, these cases be separated from other pneumonias and designated "primary atypical pneumonia, etiology unknown."[27]

This paper considers the clinical aspects of such cases and the results of attempts to establish the etiologic agent. A review of the cases of pneu-

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monia due to known viruses and rickettsias was given in the first section of this report.[28]*

Primary atypical pneumonia of unknown etiology is, in all probability, not a single disease but a syndrome that may be produced by a number of agents.[27] Nor is it a new pathologic syndrome, in spite of the numerous recent reports and the apparent increase in incidence. Positive identification of cases of atypical pneumonia, as reported in the literature, is difficult because no single criterion — clinical or laboratory — characterizes the syndrome. Moreover, clinical criteria for the diagnosis of such related infections as grippe, influenza and bronchopneumonia, which may simulate this disease, vary widely. Despite these difficulties, the entire syndrome can usually be differentiated from similar conditions of known etiology. On this basis, it is apparent that the pneumonia was seen clinically as long ago as 1872,[29, 30] and a similar pathologic picture was described at about the same time.[31, 32] With the introduction and use of roentgenography of the chest, further reports appeared, particularly in the literature dealing with tuberculosis and influenza. It seems likely that the disease was prevalent before the pandemic of influenza in 1918 and that it existed in the military forces, where it was given such names as "catarrhal fever" and "soldier's pneumonia."[33–42] In addition, almost all the reported cases of pneumonia have included a group for which the etiology either could not be determined or was thought to be one of the "higher types" of pneumococci. Clinically, many of these patients did not have typical pneumococcal pneumonia, the course of illness was unaffected by specific therapy, and the outcome was ordinarily complete recovery. Some, if not most, of these patients probably had atypical pneumonia.

Since the papers of Gallagher[1] and Bowen,[11] this type of illness has been more carefully differentiated, and cases occurring both sporadically and in small outbreaks have been reported under the variety of names listed above. Recent developments in the knowledge of viruses affecting the respiratory tract have established a preliminary basis for segregation of some of these cases etiologically, but the cause of a large number still remains unknown.

Thus, it is apparent that the characterization of atypical pneumonia is difficult and confusing, and will remain so until the etiologic problem is solved. Diagnosis can now be made only by clinical and radiologic criteria — no one of which is specific — or by exclusion. A description of the characteristics of the morbid process can only be as reliable as the diagnosis, which likewise is the basic limiting factor in the evaluation of experimental investigation. For simplicity in discussion, primary atypical pneumonia of unknown etiology will be referred to as a disease, although at present it must more accurately be considered a syndrome, possibly with multiple etiologies.

*Our attention has been called to the recent report of 2 fatal cases of lymphocytic choriomeningitis with pulmonary involvement by Smadel et al.,[91] who isolated this virus from the lungs and other tissues in both cases.

## Epidemiology

*Occurrence.* The full extent of the distribution of atypical pneumonia is not known. Its occurrence has been noted in all parts of the United States,[1, 3, 6–10, 12–16, 18, 43] in Honolulu,[11] in England[23–26] and probably on the continent of Europe.[39] These reports suggest a widespread distribution, which probably lacks confirmation only because of limited recognition. Rates of attack cannot be determined satisfactorily from the data available in the literature. The disease apparently exists sporadically and in small outbreaks.[15, 44] Bowen's[11] figures indicate a yearly attack rate varying from less than 1 to approximately 6 per 1000 in white troops during a three-year period in Honolulu. The incidence rate at Cornell University was approximately 9 per 1000 for the academic year 1937–1938.[7] Reimann[13] observed 25 cases among a hospital staff composed of 813 persons. Daniels[4] reported 13 cases in a school of about 90 girls during a six-week period — an incidence of almost 15 per cent. Cases of atypical pneumonia have comprised from less than 1 to about 6 per cent of the total admisions for respiratory diseases at different infirmaries and hospitals.[5, 10–14] It seems likely that the yearly increase in cases recently noted at several clinics may be due, in part at least, to more frequent recognition. It is possible, however, that these are epidemic forms of the disease.

*Age and sex.* The age distribution in the reported outbreaks has thus far been almost entirely limited to adolescents and young adults. Most of these outbreaks were observed in schools or military posts, where the age of the personnel is limited. The majority of the patients seen in civilian hospitals, however, have been young adults, although the span of age has varied from four to eighty years.[1–3, 12–16, 23] The limited age distribution may therefore be of significance, although recognition and opportunity for spread may be major factors. Adams[20, 22] has recently described in infants a somewhat similar virus pneumonia to which adults were apparently not susceptible. This disease, which differs in certain respects from the atypical pneumonias under discussion, is considered below. There is no rec-

ognized difference between the sexes so far as susceptibility or immunity is concerned.

*Season.* The seasonal distribution is variable, and sporadic cases apparently occur regardless of season.[9, 13-16] Many of the reported outbreaks have occurred in the late fall and winter,[3, 7, 9, 15] although the epidemic described by Reimann and Havens[14] took place between January and May, with the peak of incidence in February. Murray[9] pointed out that the majority of his cases occurred in November and December, whereas the greatest incidence of the other upper respiratory infections was noted in February and March. McKinlay and Cowan[10] also noted that an increase in upper respiratory infections did not call forth a corresponding increase in atypical pneumonia. These observations, perhaps, tend to dissociate atypical pneumonia from the common cold and other minor respiratory infections.

*Spread.* Little is known regarding the mode and manner of spread of atypical pneumonia. The general consensus is that it is transmitted by contact but is not highly communicable.[3, 9, 15, 16] Multiple cases have been seen in members of the same family or of the same household who have had opportunities for close contact.[4, 7, 13] Smiley and his co-workers[7] noted that the infectiousness of the disease was apparently not great in the absence of cough. The high incidence of infection in nurses and doctors[8, 15, 16] supports the theory of contact spread and also suggests that prolonged contact with patients may be necessary. One interpretation may be that the general resistance to atypical pneumonia is high, and as a result a large dose of the infecting agent is necessary to produce the disease. Or the infection may be more widespread than is now generally suspected, many of those afflicted presenting the symptoms and signs of a mild systemic and respiratory disease without demonstrable pulmonary lesions. Those receiving a larger primary inoculum through close contact may be likelier to develop pneumonia. The concept of mild and even inapparent or carrier infections is of considerable interest clinically and epidemiologically because of the necessity of delimiting this disease as a specific entity. A satisfactory laboratory test based on etiology will have to be obtained before this can be accomplished.

Reimann[13] noted that in a group of 5 patients who had familial contact there were 2 cases of severe infection and 3 of mild disease. In an epidemic among 813 persons at the Jefferson Hospital, he and Havens[14] described 407 cases of respiratory disease. The majority of these were mild infections, and the patients remained ambulatory. A clinical and roentgenologic diagnosis of acute tracheobronchitis was made in 6 per cent and of pneumonia in 6 per cent. These investigators believed that the patients were ill presumably of the same disease, and further stated, "Cases of the mild form far outnumbered those of the severe form, and for this reason we believe it to be misleading to apply restrictive names indicating special forms of bronchiolitis or pneumonia to cases of the severe form alone, as many have done." Gallagher[2] also noted 11 cases of mild infection, without pulmonary involvement, that epidemiologically both preceded and followed definite cases with so-called "pneumonitis." Longcope[21] has observed that patients may apparently contract a severe form of infection from those who have had a mild attack, or that the reverse may occur. It seems likely that such cases as these must be taken into consideration when one is attempting to elucidate the nature and manner of spread of atypical pneumonia.

*Incubation period.* Reliable data regarding the incubation period of atypical pneumonia are likewise lacking. Reimann and Havens[14] believed that it might be as short as one or two days, but other investigators have estimated the period to be between seven and twenty-one days, or even longer.[3, 4, 7, 9, 15, 16]

## Clinical Aspects

A clinical description of atypical pneumonia at present must be almost entirely restricted to cases presenting clinical or roentgenologic signs of pulmonary involvement. In spite of the great likelihood that related nonpneumonic or inapparent forms of infection occur, there are no reliable means by which such cases can be differentiated from other minor upper respiratory illnesses. Even in the group showing pulmonary involvement, diagnosis may not be easy. From the reports in the literature, it is difficult to accept certain cases as being consistent with atypical pneumonia, although it is entirely possible that the written descriptions convey an impression contrary to that which would be obtained on actual examination of the patient. An attempt is therefore made to present the generally accepted picture of atypical pneumonia; the significant variations that have been reported are noted.

*Onset.* The onset in the majority of cases is gradual and insidious over a period varying from one day to a week or more. Kneeland and Smetana[15] described the onset as "grippelike." Preceding or accompanying upper respiratory infections have been noted in from 50 to 75 per cent of the cases in some outbreaks,[2, 3, 9, 10] whereas in others catarrhal symptoms have been rare[13, 14] and "influenzalike" symptoms absent.[4]

The onset has been described as sudden or abrupt by Daniels[4] in all his cases, and by Murray[9] in about one fourth of his cases. It is rarely so abrupt and dramatic as that in pneumococcal pneumonia.

*Symptoms.* The presenting symptoms are ordinarily quite uniform early in the disease, regardless of the subsequent severity and course of the illness. Fever, cough, malaise, headache and chilliness are almost constant complaints. The temperature may be at any level between 99 and 105°F., or more, but is usually between 100 and 103°F. Cough, at this stage, is very distressing to the patient. It is dry and may occur in paroxysms, which are difficult to control. Substernal pain or soreness and tenderness of the abdominal muscles frequently result from tracheal irritation and cough. The cough may be productive, however, at the onset or early in the course.[9, 16] The sputum is mucopurulent and may be blood streaked, but is not rusty or suggestive of prune juice. Malaise, aches and pains, and prostration may be out of proportion to the general appearance of the patient. Headache is often severe and is frequently frontal or periorbital, but may be general or localized anywhere. Sensations of chilliness and shivering usually alternate with periods of feverishness, but shaking chills and rigor seldom occur. The throat may be dry or sore before or at the time of onset, but usually sore throat does not persist beyond the first few days of illness. Drenching sweats occur in some cases.[7, 9, 13, 14] Gastrointestinal symptoms are usually not a feature. Other symptoms, such as stiff neck, vertigo, abdominal distention, dyspnea, cyanosis and mental confusion and disorientation, occur rarely or are seen later in the course of the disease.

*Physical signs.* Physical examination early in the disease usually reveals little that is abnormal. Fever is almost constantly present, but the majority of the patients do not appear to be so ill as their fever or subjective complaints would warrant. Some patients appear moderately or severely ill, with evident prostration and, occasionally, dyspnea and cyanosis. Aside from pharyngeal injection and, rarely, a palpable spleen,[9] the examination is negative. The pulse rate ordinarily is within normal limits or low. Respirations are usually normal. Pulmonary signs, if present, are generally limited to fine or medium moist rales occurring late in inspiration.

*Laboratory findings.* The white-cell count is normal in almost all cases early in the disease. Both leukopenia and leukocytosis are infrequent in the absence of other contributing causes. The sedimentation rate may be elevated, but other laboratory tests are usually negative.

*X-ray findings.* The first evidence of pulmonary involvement is usually obtained by roentgenologic examination of the chest. Lesions may be apparent on admission and are almost always found within the first few days of the disease. The character, size and location of the lesion are variable.[4, 9, 11, 15, 16, 25, 26, 45, 46] In the majority of patients, the first change noted is an increase in the size of one or both hilar shadows, followed by an infiltration, which extends outward from the hilum toward the periphery of the lung fields, often in the shape of a fan or wedge, and fades out gradually into the normal lung parenchyma. Origin of the lesion at the periphery of the lung has not been described in typical cases. Most frequently, the lesion is found in one of the lower lobes, but it may occur anywhere. Bilateral involvement is not uncommon, and is found in 20 per cent or more of the cases.[8] The process may spread to the adjoining lobes and, infrequently, is very extensive, involving all, or almost all, the lobes. Usually, the infiltration is soft, either mottled or homogeneous, and denser near the hilum. It is rarely so dense and circumscribed as that in pneumococcal pneumonia, and seldom does it occupy more than a portion of a lobe.

A number of variations in the radiologic picture have been noted, which may be striking. A fairly well-localized, but not sharply defined, lesion may be found in the lower lobes, particularly in one or the other cardiophrenic angle. The process may be light, diffuse and mottled in any portion of the lung field. There may be multiple small areas of soft infiltration that increase in size and become irregularly confluent; or there may be areas of diffuse, rather coarse mottling in foci varying from 2 to 5 mm. in diameter — the "disseminated focal pneumonia" of Scadding,[25] which may be impossible to distinguish from tuberculosis. Kornblum and Reimann[45] have described the picture of "acute tracheobronchitis," which they believe represents the same infectious process, as a bilateral increase in the hilar and trunk shadows, with indistinct outlines, soft mottling about the hilum and generally hazy lung fields. Similar findings have been noted in influenza.[47]

Resolution of the process is usually slow, but the shadows may at times be quite transitory.[26, 46] The process often clears from the periphery of the lesion, which becomes more mottled and then fades. Increase in the size of the hilar shadows may persist for several weeks.

Thus, the radiographic picture, although fairly characteristic, may show sufficient variations to be confused with that of pneumococcal pneumonia, bronchopneumonia, acute bronchitis, tuberculosis, pulmonary abscess, acute bronchiectasis, metastatic

infiltration and, of course, the known virus and rickettsial diseases that involve the lung.[28]

*Course.* The course of the disease is generally mild, although cases of varying severity and even fatal ones have been reported.[13, 15, 16] Therefore, the course will be described separately for mild, moderately severe and severe types; one should bear in mind that the differences are chiefly of degree and not of kind.

Patients suffering from the *mild form* of illness usually show the maximum rise in temperature within three days after onset. The temperature may vary from 99 to 105°F.; it may be sustained but is frequently swinging. Defervescence is usually slow, by lysis, for the next few days. The average febrile period is seven or eight days, although it varies considerably. Allen,[12] for example, reported that 68 per cent of his cases had fever for three to eleven days, whereas 12 per cent were febrile for more than twenty days. Headache and chilliness usually persist throughout the febrile period, and the cough ordinarily becomes productive as the disease progresses. Cyanosis and dyspnea are rare. Malaise, lassitude and fatigue often persist several days or weeks after the acute stage of the illness, whereas sore throat is usually present for only the first few days. Unusual sweating has been noted in certain of the outbreaks.[9, 13] Bradycardia is common, and the respiratory rate is frequently normal or only slightly elevated.

Physical signs are frequently limited to rales over the involved area, often appearing after three or four days of illness or even longer. In most cases, the rales are fine or medium moist and sticky, and occur late in inspiration, although in some cases they have been described as coarse and explosive.[16] During the later stages, when the cough becomes productive, coarse, wet rales and rhonchi may be present. Dullness may be noted, but it is often slight and little more than an increased sense of resistance. Abnormal breath sounds, increased tactile fremitus and the other signs of consolidation are infrequent, but may be found in from 13 to 15 per cent of the cases.[2, 3, 9] Spread of the lesion may be detected by physical or radiologic examination and may be associated with exacerbation of symptoms and fever. Other abnormal physical findings are not frequent. Splenomegaly has been noted in a few cases[9]; abdominal distention is unusual. Herpes and pleural effusion are rare.[9, 15] The ordinary laboratory tests give results within normal limits throughout the course. Ordinarily, the physical signs and objective evidences of illness are gone within two or three weeks after onset, but complete subjective recovery may not occur for four to six weeks.

Complications are not commonly observed, but those described are pharyngitis, tonsillitis, sinusitis, otitis media, pneumonia and empyema due to the hemolytic streptococcus,[10] urticaria, ulcerations on the palate and persistent productive cough suggesting bronchiectasis.

The *moderately severe cases* differ in no significant particulars from the mild cases, except that the patients feel and look sicker. The progress of the disease may be more rapid. Cough and headache may be more pronounced. Dyspnea and cyanosis may be present. The temperature may persist longer and at a higher level, and may be associated with tachycardia and an increased respiratory rate. Spread of the lesion and relapses may occur. There may be little or no correlation between the clinical severity of the infection and the extent of pulmonary involvement by x-ray or physical examination. Not infrequently, the total white-cell count becomes elevated as the disease progresses, without any apparent evidence of secondary bacterial invasion. Complications may be somewhat more frequent, but are of the same type in these cases as in the mild ones.

In the *severe form*,[14–16,21] patients usually have an onset of infection that is similar to that described for the mild cases. The symptoms are more pronounced, however, and the progress of the disease to a severe state may be rapid. Fever, severe headache and persistent cough are the outstanding features. Prostration is marked. Dyspnea and cyanosis are usually present in these cases, and the breathing may be rapid, obstructive and asthmatic. Epistaxis, chills and sweating may occur. Drowsiness, meningismus and coma have been described. The temperature may remain elevated, as in typhoid fever, or may be swinging or "septic." Relapses, giving a biphasic or saddleback temperature curve, are not uncommon. The pulse may be relatively slow, but more frequently it is rapid and more in proportion to the fever than in the milder cases.

Examination of the chest physically and roentgenologically reveals involvement of variable extent that frequently spreads over a considerable portion of the lung fields. Moist rales and rhonchi are the outstanding features, however, and evidence of dense consolidation is not the rule. Other associated findings are polyarthritis, erythematous rash, pleural effusion, thrombophlebitis, evidence of myocardial involvement and signs of involvement of the central nervous system. These findings are rare, however, and, as mentioned above, it is difficult to be certain that they are related to the same process in the absence of specific diagnostic criteria based on etiology.

Laboratory studies in these severe cases may show a moderate secondary anemia and a gradual elevation of the white-cell count as the disease progresses. The urine may show albumin in proportion to the fever. The sedimentation rate is

elevated.[15] In a few cases, liver damage has been suspected on the basis of slight jaundice, reversal of the albumin-globulin ratio, bromsulfalein retention and a shifting Wassermann reaction.[15]

The duration of the acute illness is usually two or three weeks, but it may be six to eight weeks or even longer before complete recovery has occurred and the chest is clear by physical and x-ray examination. Although complete recovery is usual, death may result from the disease itself, from secondary bacterial invasion or from the infection superimposed on pre-existing organic disease. McKinlay and Cowan[10] observed a fatal case complicated by pneumonia and empyema due to the hemolytic streptococcus. In a series of 40 cases described by Longcope,[16, 21] there were 3 fatal cases, 2 of which were in patients with chronic rheumatic heart disease with mitral stenosis and insufficiency.

### *Atypical Pneumonia in Infants and Children*

Although the outbreaks of atypical pneumonia described in the literature have been almost entirely limited to adolescents and young adults, it seems probable that the disease is not confined to this age group. Several investigators[12, 23, 26, 46] have described apparently identical illnesses in children between the ages of four and nine years. Recently, Adams, Grier, Evans and Beach[20, 22] have described two epidemics of respiratory disease in young infants up to thirty-two weeks of age. Low-grade fever, cough, dyspnea and cyanosis were the outstanding features. The only characteristic signs in the chest were widely scattered fine rales. Radiologic examination revealed a patchy infiltration, particularly in the upper lobes. Resolution of the process was slow. The average case fatality rate was 20 per cent, but the rate was especially high in those infants who had been born prematurely (82 per cent). Somewhat similar types of illness have been described previously, usually following measles, pertussis or other conditions.[17, 48, 49]

## Pathology

Knowledge of the pathology of atypical pneumonia is limited because of the low mortality of the infection. The chief pathological features of the fatal cases reported by Kneeland and Smetana[15] and by Longcope[16, 21] are those of a patchy, hemorrhagic, interstitial bronchopneumonia associated with acute bronchitis and bronchiolitis. Grossly, there are areas of atelectasis and emphysema, small areas of red or gray consolidation, which in some places have apparently become confluent, and reddened bronchi filled with mucoid or purulent exudate. Microscopically, the alveolar exudate may be hemorrhagic or mononuclear in some areas, whereas in others there is evidence of organization. The alveolar septums may be infiltrated with mononuclear cells and may later show thickening, with a decrease in the size of the alveolar spaces. The process may be most marked in the alveoli surrounding the bronchi and bronchioles. The walls of the bronchi and trachea show necrosis and infiltration with polymorphonuclear leukocytes, and their lumens are usually filled with exudate containing a predominance of these cells. Edema fluid in the alveoli and frothy pink material in the bronchi have been described in one case,[16] which was complicated by chronic rheumatic heart disease and may have been the result of congestive failure. Necrosis and cellular infiltration of the walls of the pulmonary artery[15] and of its smaller radicles[16] have been noted. Acute splenic tumor and focal hepatic necroses have also been described.[15] No inclusion bodies have been found in these cases.

It is interesting to note the similarity of the above description to those given for bronchopneumonia or "interstitial pneumonia,"[29, 31, 32] "purulent bronchitis,"[33] influenza, psittacosis and other known virus diseases,[28] pneumonia due to the influenza bacillus[50] and pneumonia complicating measles, whooping cough and other diseases in man and animals.[17, 49, 51]

Essentially the same pathologic processes were found by Adams and his co-workers[20, 22] in the lung of infants dying of an acute epidemic respiratory disease mentioned earlier in the paper. In addition, these investigators noted acidophilic intracytoplasmic inclusion bodies in the bronchial epithelial cells. Similar inclusions were found in cells obtained by swabbing of the throats of infected infants, and of control infants and adults having contact with these cases. The presence of inclusion bodies is suggestive evidence of infection with a virus, but conclusive proof of virus etiology can be obtained only by the isolation of the virus and demonstration of its specific relation to the disease. Thus, intracytoplasmic or, more frequently, intranuclear inclusions have been found in the epithelial cells of infants and children following measles, influenza, whooping cough and a number of related infectious and noninfectious processes,[17, 48, 49] but an etiologic relation has not been demonstrated satisfactorily.

## Etiology

The etiology of atypical pneumonia has not been established satisfactorily. As pointed out above, this clinical syndrome may be produced by a number of known bacteria and viruses, and yet in the majority of the reported outbreaks in which studies were made, none of these agents were identified with the disease.

The usual laboratory procedures have yielded entirely negative results. Blood cultures are ordinarily sterile.[16] Agglutinins are not demonstrable for the bacilli of typhoid fever, undulant fever, tularemia and suipestifer infection, and blood smears reveal no malarial parasites.[8, 16] Cultures of the sputum show the usual throat flora: *Streptococcus viridans, Neisseria catarrhalis*, staphylococci, *Str. haemolyticus*, diphtheroids and influenza bacilli.[1-4, 7, 8, 10, 13-16, 21, 25, 52] Pneumococci have been found in more than half the cases by some investigators[19] and infrequently by others,[3, 14, 15] but in practically all the organisms are of the so-called "higher types," which are less pathogenic and more commonly found in carriers. Kneeland and Smetana[15] considered the distribution of bacteria present in the respiratory tract of their cases to be essentially the same as that of normal persons. No tubercle bacilli or fungi are demonstrable.[16, 25] The appearance of hemolytic staphylococci or streptococci in the sputum late in the disease as possible secondary invaders is probably not frequent, since it has been noted in only 3 cases.[16, 52] Adams and his co-workers[20, 22] reported no significant bacteriologic findings in their cases in infants.

A number of attempts have been made to isolate rickettsias or viruses from these cases. From Reimann's[13] cases, Stokes, Kenney and Shaw[53] and Francis and Magill[54] obtained an agent that produced illness and pulmonary lesions in ferrets and mice for a few passages, but then apparently became less virulent and was lost. Neither the influenza nor the psittacosis virus was isolated, and the patients did not develop complement-fixing antibodies for the influenza virus.[14] Enders, Sullivan, Hammon and Meakins[55] examined blood, sputum and nasopharyngeal washings from 11 of the cases reported by Murray,[9] but in no case was a virus obtained. Brown[56] was unable to isolate rickettsias or a virus from various specimens, including pulmonary tissue from the fatal cases reported by Longcope.[16, 21] As noted above, no inclusion bodies were seen in these cases. Negative results were also obtained in a variety of animals, and in chick embryos with autopsy material from the fatal cases in infants studied by Adams, Green, Evans and Beach,[22] although inclusion bodies were seen. Blood and pharyngeal washings from 6 of Daniels's[4] cases were inoculated by Dyer and Topping[57] into mice, guinea pigs and chick embryos with negative results.

Weir and Horsfall[58] have reported the isolation in the mongoose and in chick embryos of a filterable agent obtained from each of 4 patients with "acute pneumonitis." Production of pulmonary lesions in mongooses was somewhat irregular, since some animals were apparently resistant to infection, and serial passage did not increase the virulence of the agent. By a rather laborious passage technic, it was found that the agent, when mixed with convalescent serums of the patients, produced a lower percentage of pulmonary lesions in the mongoose than when acute serums were similarly employed, indicating the development of neutralizing antibodies. A large variety of animals, including monkeys, were resistant to inoculation with the original material from the patients, as well as with pulmonary tissue from the infected mongoose. The agent was apparently not related to other known viruses producing respiratory disease.

Further work is necessary to clarify the etiologic situation in atypical pneumonia. Until this has been accomplished, diagnosis of the disease will remain uncertain. Differentiation should be made as completely as possible on the basis of laboratory tests to exclude the known viruses that can cause the same clinical picture, such as those of influenza A and B, psittacosis, meningopneumonitis,[28, 59] ornithosis and rickettsias. Other conditions, such as tuberculosis, typhoid fever, undulant fever, pneumococcal pneumonia, coccidiodomycosis, bronchiectasis, cancer, pulmonary infarction and atelectasis, must, of course, be considered in the differential diagnosis.

### Treatment and Prevention

The treatment of atypical pneumonia at present is entirely supportive or symptomatic, since no specific measures are known. The diet may be unrestricted or determined by the patient's appetite. The fluid intake, either orally or parenterally, should be maintained at 3000 to 4000 cc. per day, or more during hot weather. Adams and his co-workers[22] have stated, however, that infants with "primary virus pneumonitis" do not tolerate parenteral fluids well. Opiates, particularly codeine sulfate in ½-gr. or 1-gr. doses, are of value for cough, headache and generalized aching, but suppression of these symptoms may be difficult. Expectorants may be helpful when sputum is scant. Steam inhalations, with or without tincture of benzoin, or an increase in the humidity of the ward may give some relief. Abdominal binders and an ice cap may also be helpful. Reimann and Havens[14] recommend that acetylsalicylic acid, acetophenetidin and aminopyrine be avoided because of the diaphoretic action of these drugs, particularly in cases in which sweating is an annoying symptom of the disease. Oxygen therapy, a tent or a nasal catheter being employed, usually relieves dyspnea and cyanosis. Postural drainage may be of value if the cough becomes productive

of large amounts of sputum in the later stages of illness. Sprays or gargles of physiologic saline solution or weak sodium perborate solution may be employed, and a spray of 1 per cent aqueous solution of ephedrine may be used to relieve nasal obstruction. Enemas should be employed as indicated.

Transfusions have been recommended.[8, 22] Kneeland and Smetana[15] have given a transfusion from a convalescent donor in 1 case, but the value of this specific therapy has not yet been established. The various sulfonamide drugs have been used in a considerable number of cases,[3, 4, 14, 16, 22] without any significant effect on the course of the disease. Indeed, in some cases, the reactions to these drugs have materially increased the discomfort of the patients.[14] Pneumococcal antiserums have been tried in a few cases, without evident success.[14] In most cases, a prolonged period of convalescence is required. Complications should be treated as indicated.

Only general preventive measures are available in attempts to stop the spread of atypical pneumonia. The infection is apparently not highly communicable, but the large number of cases occurring in medical personnel caring for these patients indicates contact spread, possibly by droplet infection. Strict isolation of the patients is recommended.[14, 21] Masks and gargles may be of value.[60] Prevention by immunization must await the isolation of the etiologic agent.

## References


1. Gallagher, J. R. Bronchopneumonia in adolescence. *Yale J. Biol. & Med.* 7:23-40, 1934.
2. *Idem.* Acute pneumonitis: a report of 87 cases among adolescents. *Yale J. Biol. & Med.* 13:663-678, 1941.
3. *Idem.* Acute pneumonitis: report of an epidemic. *Yale J. Biol. & Med.* 13:769-781, 1941.
4. Daniels, W. B. Bronchopneumonia of unknown etiology in a girls' school. *Am. J. M. Sc.* 203:263-276, 1942.
5. Bock, A. V. Clinical observations, complications and treatment of acute respiratory tract infections. *Ann. Int. Med.* 12:317-322, 1938.
6. Rainey, W. G., and Burbidge, J. R. Acute pneumonitis or atypical pneumonia. *Journal-Lancet* 59:101-104, 1939.
7. Smiley, D. R., Showacre, E. C., Lee, W. F., and Ferris, H. W. Acute interstitial pneumonitis: a new disease entity. *J. A. M. A.* 112:1901-1904, 1939.
8. Maxfield, J. R., Jr. Atypical pneumonia with leukopenia. *Texas State J. Med.* 35:340-346, 1939.
9. Murray, M. E., Jr. Atypical bronchopneumonia of unknown etiology: possibly due to a filterable virus. *New Eng. J. Med.* 222:565-573, 1940.
10. McKinlay, C. A., and Cowan, D. W. Acute respiratory infections including lobar pneumonia and atypical pneumonia in a young adult group. *Journal-Lancet* 61:125-133, 1941.
11. Bowen, A. Acute influenza pneumonitis. *Am. J. Roentgenol.* 34:168-174, 1935.
12. Allen, W. H. Acute pneumonitis. *Ann. Int. Med.* 10:441-446, 1936.
13. Reimann, H. A. An acute infection of the respiratory tract with atypical pneumonia: a disease entity probably caused by a filterable virus. *J. A. M. A.* 111:2377-2384, 1938.
14. Reimann, H. A., and Havens, W. P. An epidemic disease of the respiratory tract. *Arch. Int. Med.* 65:138-150, 1940.
15. Kneeland, Y., Jr., and Smetana, H. F. Current bronchopneumonia of unusual character and undetermined etiology. *Bull. Johns Hopkins Hosp.* 67:229-267, 1940.
16. Longcope, W. T. Bronchopneumonia of unknown etiology (variety X). A report of thirty-two cases with two deaths. *Bull. Johns Hopkins Hosp.* 67:268-305, 1940.
17. Goodpasture, E. W., Auerbach, S. H., Swanson, H. S., and Cotter, E. F. Virus pneumonia of infants secondary to epidemic infections. *Am. J. Dis. Child.* 57:997-1011, 1939.
18. Moss, J. Some features of "virus pneumonia." *North Carolina M. J.* 3:27-30, 1942.
19. Bayne-Jones, S. Virus pneumonia. *Connecticut M. J.* 4:258, 1940.
20. Adams, J. M. Primary virus pneumonitis with cytoplasmic inclusion bodies: study of an epidemic involving thirty-two infants, with nine deaths. *J. A. M. A.* 116:925-933, 1941.
21. Longcope, W. T. Pneumonitis or virus pneumonia. *Practitioner* 148:1-8, 1942.
22. Adams, J. M., Green, R. G., Evans, C. A., and Beach, N. Primary virus pneumonitis: a comparative study of two epidemics. *J. Pediat.* 20:405-420, 1942.
23. Gill, A. M. Pneumonitis. *Brit. M. J.* 1:504-507, 1938.
24. Maxwell, J. Pneumonitis. *Lancet* 2:239-241, 1938.
25. Scadding, J. G. Disseminated focal pneumonia. *Brit. M. J.* 2:956-959, 1937.
26. Ramsay, H., and Scadding, J. G. Benign broncho-pulmonary inflammations associated with transient radiographic shadows. *Quart. J. Med.* 8:79-95, 1939.
27. Official Statements: Primary atypical pneumonia, etiology unknown. *War Med.* 2:330-333, 1942.
28. Finland, M., and Dingle, J. H. Virus pneumonias. I. Pneumonias associated with known nonbacterial agents: influenza, psittacosis and Q fever. *New Eng. J. Med.* 227:342-350, 1942.
29. Woillez, E. J. *Traité clinique des maladies aiguës des organes respiratoires.* 656 pp. Paris: Adrien Delahaye, 1872.
30. Leichtenstern, O. Influenza und Dengue. In Nothnagel, H. *Specielle Pathologie und Therapie.* Vol. 4, Pt. 1. Vienna: Alfred Hölder, 1896. Pp. 1-195.
31. Bartels. Bemerkungen über eine im Frühjahre 1860 in der Poliklinike in Kiel beobachtete Masernepidemie, mit besonderer Berücksichtigung der dabei vorgekommenen Lungenaffectionen. *Virchows Arch. f. path. Anat.* 21:65-84, 1861.
32. Delafield, F. The pathology of broncho-pneumonia. *Boston M. & S. J.* 111:484-487, 1884.
33. Hammond, J. A. B., Rolland, W., and Shore, T. H. G. Purulent bronchitis: a study of cases occurring amongst the British troops at a base in France. *Lancet* 2:41-45, 1917.
34. Hesse, W. Über zentrale Pneumonia und ihre Bedeutung für die zentrale Entstehung der Pneumonie. *München. med. Wchnschr.* 65:1125-1128, 1918.
35. Liebman, E., and Schinz, H. R. Über das Röntgenbild der Influenzapneumonie. *Ztschr. f. klin. Med.* 90:345-375, 1921.
36. Opie, E. L., Blake, F. G., Small, J. C., and Rivers, T. M. *Epidemic Respiratory Disease.* 402 pp. St. Louis: C. V. Mosby Co., 1921.
37. Roentgenology. In *The Medical Department of the United States Army in the World War.* Vol. 9. *Communicable and Other Diseases.* 628 pp. Washington: Government Printing Office, 1928. Pp. 152-154.
38. Eimer, K., and Kestermann, E. Die Bedeutung des Röntgenbildes für die Prognose der Grippe-Bronchopneumonie. *Ztschr. f. klin. Med.* 118:323-336, 1931.
39. Jeanneret, R., and Famé, F. L'image radiologique de la broncho-pneumonie grippale. *Rev. méd. de la Suisse Rom.* 51:418-421, 1931.
40. Thums, K. Über akute Miliartuberkulose. *Beitr. z. Klin. d. Tuberk.* 78:273-282, 1931.
41. Kellner, F. Die Bedeutung pneumonischer Prozesse für die Klinik der Tuberkulose. *Beitr. z. Klin. d. Tuberk.* 81:639-658, 1932.
42. Leitner, J. Über flüchtige Lungeninfiltrate. *Ztschr. f. Tuberk.* 66:226-232, 1932.
43. Miller, F. N., and Hayes, M. G. Bronchopneumonia of mild severity at University of Oregon. *Northwest Med.* 38:12-14, 1939.
44. Finland, M., Brown, J. W., and Barnes, M. W. Immune reactions of carriers and noncarriers of type-specific pneumococci: a bacteriological and immunological study of hospital contacts. *Am. J. Hyg.*, Sect. B, 32:24-37, 1940.
45. Kornblum, K., and Reimann, H. A. The roentgenological aspects of an epidemic of acute respiratory tract infection. *Am. J. Roentgenol.* 44:333, 1940.
46. Nicholas, F. G., and Agassiz, C. D. Radiography in pneumonia: diagnosis of complications and atypical forms. *Lancet* 2:705-709, 1938.
47. Stuart-Harris, C. H., Andrewes, C. H., and Smith, W. A study of epidemic influenza: with special reference to the 1936-7 epidemic. 151 pp. *Medical Research Council Special Report Series* No. 228. London: His Majesty's Stationery Office, 1938.
48. Goodpasture, E. W., and Talbot, F. B. Concerning the nature of "protozoa-like" cells in certain lesions of infancy. *Am. J. Dis. Child.* 21:415-425, 1921.
49. McCordock, H. A., and Smith, M. G. Intranuclear inclusions: incidence and possible significance in whooping cough and in a variety of other conditions. *Am. J. Dis. Child.* 47:771-779, 1934.
50. Brannan, D., and Goodpasture, E. W. The pathology of pneumonia caused by Bacillus influenzae during an inter-epidemic period. *Arch. Int. Med.* 34:739-756, 1924.
51. McCordock, H. A., and Muckenfuss, R. S. The similarity of virus pneumonia in animals to epidemic influenza and interstitial bronchopneumonia in man. *Am. J. Path.* 9:221-252, 1933.
52. McKinlay, C. A. Acute diffuse bronchiolitis: report of a case. *Journal-Lancet* 59:90, 1939.
53. Stokes, J., Jr., Kenney, A. S., and Shaw, D. R. A new filterable agent associated with respiratory infections. *Tr. & Stud., Coll. Physicians, Philadelphia* 6:329-333, 1939.
54. Francis, T., and Magill, T. P. Quoted by Reimann.[13]
55. Enders, J. F., Sullivan, E. R., Hammon, W. D., and Meakins, J. L. Cited by Murray.[9]
56. Brown, T. M. Cited by Longcope.[21]
57. Dyer, R. E., and Topping, N. H. Quoted by Daniels.[4]
58. Weir, J. M., and Horsfall, F. L., Jr. The recovery from patients with acute pneumonitis of a virus causing pneumonia in the mongoose. *J. Exper. Med.* 72:595-610, 1940.
59. Eaton, M. D., Beck, M. D., and Pearson, H. E. A virus from cases of atypical pneumonia: relation to the viruses of meningopneumonitis and psittacosis. *J. Exper. Med.* 73:641-654, 1941.
60. Andrewes, C. H. Epidemic influenza. *Lancet* 1:589-591, 1939.
61. Smadel, J., Green, R. H., Paltauf, R. M., and Gonzales, T. A. Lymphocytic choriomeningitis: two human fatalities following an unusual febrile illness. *Proc. Soc. Exper. Biol. & Med.* 49:683-686, 1942.

# CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

## CASE 28361

### PRESENTATION OF CASE

A forty-year-old man was admitted to the hospital because of bouts of abdominal pain.

Five months before admission, the patient experienced a sudden attack of pain without anorexia or nausea, sharply localized to the right lower quadrant. This episode lasted three days. No change in bowel habits had occurred, and on examination, there was only mild tenderness in the right lower quadrant. A month later, similar symptoms recurred, and an "infected appendix" was removed at a community hospital. At operation, an inflammatory mass of undescribed size was attached to the ileum several inches from the ileocecal valve. Following this, the patient made an uneventful recovery. Five weeks later, symptoms recurred, but at this time, the patient complained of generalized gas pains and soreness in the epigastrium. These were relieved by an enema, but recurred once during the succeeding month with an associated left-lower-quadrant pain. This time, relief was obtained from a topical application of heat. No changes in stool habits or characteristics were noted.

The family and past histories were irrelevant.

Physical examination revealed a rather thin man in no obvious distress. The heart and lungs were normal. A firm, movable "egg sized" tender mass was felt in the right lower quadrant several inches to the side of the umbilicus. Rectal examination was negative.

The blood pressure was 125 systolic, 80 diastolic. The temperature was 98.6°F., the pulse 90, and the respirations 20.

Examination of the blood revealed a hemoglobin of 14 gm., and a white-cell count of 9800 with 88 per cent polymorphonuclears, 8 per cent lymphocytes, 2 per cent monocytes and 2 per cent eosinophils. The blood Hinton reaction was negative. Urine and stool examinations were negative.

A barium enema passed to the cecum without delay and entered the terminal ileum. Approximately 6 cm. from the ileocecal valve, there was a localized area of ulceration on the lateral wall of the terminal ileum, with rather sharp margins. In addition to the area of ulceration, a soft-tissue mass appeared to be pressing into the lumen of the bowel. There was a moderate amount of mucosal swelling. The ileum proximal to the lesion was not dilated. A single diverticulum was seen in the midtransverse colon.

Operation was performed on the ninth hospital day.

### DIFFERENTIAL DIAGNOSIS

DR. EDWARD HAMLIN, JR.: I think we had better start with the x-ray films.

DR. AUBREY O. HAMPTON: The radiologist cannot often give a report so definite as this, but these films show why he was so certain that the ileum was ulcerated — there is a notchlike projection here simulating a gastric ulcer. It is a deep ulcer, 1 cm. in diameter, and there is an area of rigidity around it that might also be shallowly ulcerated, 3.5 to 4 cm. in width. The reason the radiologist said that there was a mass pressing into the ileum is that there do seem to be a large number of mucosal folds in the area of this lesion, which are not exactly normal.

DR. HAMLIN: Could the effect be produced by rigidity of the bowel?

DR. HAMPTON: I think the bowel must have been rigid near the ulcer over an area about 3.5 cm. in length.

DR. HAMLIN: The patient complained of intermittent pain, some of which might be classed as local peritoneal irritation, some of which was quite likely due to low-grade intestinal obstruction, and some of which I cannot account for. I should rather like to know — he is described as a thin man but we are not told whether he had loss of weight or increased fatigability — whether or not this was a chronic lesion that had produced effects. The examination tells us nothing more than that there was a mass in the right lower quadrant. The laboratory data reveal nothing of any significance except that there was no evidence of really acute inflammation, although perhaps one could call this a low-grade inflammatory process. The written x-ray report puzzled me more than anything else. One other thing that bothered me was the description of the inflammatory mass noted at previous operation at the time of appendectomy because of the use of the word "attached." It sounds rather like a tumor that was protruding from the wall of the intestine.

Several conditions might have been responsible for this lesion. The first thing I thought of was the question of foreign body. A foreign body, which impinged on the mucosa of the bowel and became imbedded, could produce such a low-grade inflammatory process, although Dr. Hampton's comments make it seem rather less likely. The chief objection is the elapsed period of five

months since the onset of symptoms, which is rather a long time to associate with a foreign body in such intimate contact with the bowel.

The patient had a tumor. Could the tumor have been neoplastic? The carcinomas and carcinoids of the small bowel are rare. The one or two that I have seen certainly produced no picture such as this. They are mostly annular and constricting and much more likely to cause obstruction than ulceration of this nature. The one tumor that seems most likely to produce a picture of this sort rather than any other is lymphoma, and that I cannot exclude. One would think that lymphoma would be more likely to cause a secondary anemia and blood in the stools, which this man did not have.

A Meckel's diverticulum containing gastric mucosa occurred to me as a possibility. The lesion is certainly rather closer to the cecum than one would expect, and a study that Wallace[1] made in this hospital revealed that when the symptoms from a Meckel's diverticulum could be attributed to the presence of gastric mucosa they resulted before the age of twenty, and this man was well beyond that. Accordingly, we can probably exclude any effect of a Meckel's diverticulum.

When one considers the diseases of the ileum, one immediately thinks of ileitis. Could this have been an atypical form of regional ileitis? Crohn and Berg[2] state that blood almost invariably is noticed in the bowel movements. However, of the 33 cases of regional ileitis in the series reported by Warren and Miller[3] in this hospital, only 2 showed blood in the stools. Diarrhea is one of the most important symptoms of regional ileitis; yet in this same series, 6 patients had no evidence of diarrhea when the diagnosis of ileitis was made. Obstruction is not an obstacle, because in studies of ileitis there may be no x-ray evidence of obstruction such as one would expect from constriction of the inflammatory lesion. The one factor that is perhaps more of an obstacle than any of the others is that fistulas did not result following the appendectomy. All the fistulas that have been seen in this hospital in cases of regional ileitis have resulted from operation.

There are several other lesions or diseases that might possibly produce this picture, most of which are rare and are not worth the time to discuss. I cannot exclude a lymphoma or an atypical regional ileitis, and of the two I should favor the latter.

Dr. Hampton: I was just about to say that I do not believe we have seen anything similar to this in regional ileitis. A local single ulceration would be most unique, I should think; and then it does have the picture of a tumor by x-ray — the shellike margin around the area of stiffening. This penetrating ulcer simulating a gastric ulcer is the part that we did not like because we had not seen such a picture. It seemed as if there might be a "nigger in the woodpile," but I think the diagnosis on x-ray study was lymphoma.

A Physician: What would you say about carcinoid?

Dr. Hampton: It does not produce ulceration.

Dr. Tracy B. Mallory: I should emphatically say that we have never seen ulceration with carcinoid in the ileum. On the other hand, carcinoid frequently involves regional lymph nodes and would account for pressure from an extrinsic lesion in addition to signs of intrinsic mass.

Dr. Leland S. McKittrick: We thought there was a possibility that there was no ulcer — in other words, that this was infolding of the mucosa.

Dr. Hampton: No one suspected that. We thought it must be ulcerated.

Dr. McKittrick: Just to be sure of the written impression of the X-ray Department, it says: "This can be either inflammatory process or tumor. If tumor is the cause, the most likely possibility would be carcinoma or carcinoid." That may not represent the impression of the X-ray Department, but that is the written interpretation.

Dr. Hampton: That is the impression of an individual. The majority of the department staff did not agree with him.

Dr. McKittrick: When this man was sent to me, I thought he had regional enteritis from the story. I cannot find my preoperative diagnosis, and I am not absolutely sure of the diagnosis we operated under, but I think it was carcinoma even though the location was unusual. There is no reason why it could not occur there, and the x-ray picture was entirely consistent, as was the clinical story. The patient did have a lesion that was perfectly characteristic of a carcinoma — a firm hard indurated mass, classic in every way. The unusual part about it was the large mass of nonbroken-down lymph nodes extending along the root of the mesentery. Further exploration showed that the liver and spleen were normal; there was nothing else within the abdominal cavity that I could find. We did a right colectomy.

A Physician: Including the terminal ileum, of course?

Dr. McKittrick: Yes; the terminal ileum and the right colon around to the midtransverse colon were removed. That was the only way we could include the lymph nodes at the root of the mesentery without interfering with the blood supply.

### Clinical Diagnosis

Carcinoma of terminal ileum?
Terminal ileitis?

### Dr. Hamlin's Diagnosis

Regional ileitis?
Lymphoma?

### Anatomical Diagnosis

Malignant lymphoma, lymphoblastic type, of ileum.

### Pathological Discussion

Dr. Mallory: We were puzzled by this specimen when it came to the laboratory. When it was opened, there was an ulcerative tumor of the bowel looking like carcinoma, and a mass of lymph nodes in the mesentery, some of them matted together. Cutting across this mass of nodes, we found them to consist of soft pinkish tissue that showed no signs of necrosis or breaking down, so that the nodes were very unlike carcinoma and very suggestive of lymphoma. On the other hand, our experience with lymphoma in the bowel is that the regional lymph nodes are very seldom involved even when grossly enlarged. They ordinarily show simple hyperplasia and no lymphomatous infiltration, whereas it was obvious that these nodes were neoplastic. Microscopic examination showed that it was lymphoma of an undifferentiated lymphoblastic type, and the same picture was present both in the bowel wall and in the regional lymph nodes.

Since operation, this patient has been given intensive x-ray treatment. I do not know whether the tumor has recurred.

Dr. McKittrick: I heard from the patient's physician recently. The patient was reported to be doing well six months after the operation.

Dr. Mallory: A significant proportion of these lymphomas of the bowel, of course, do remarkably well after resection. We have cases that have run seven, nine and eleven years after resection, and they are therefore well worth operating on.

### References

1. Wallace, R. H. Personal communication.
2. Crohn, B. B., and Berg, A. A. Right-sided (regional) colitis. *J. A. M. A.* 110:32-38, 1938.
3. Warren, R., and Miller, R. H. Regional enteritis. *New Eng. J. Med.* 226:589-593, 1942.

## CASE 28362

### Presentation of Case

A forty-four-year-old lumber salesman was admitted to the hospital because of periumbilical pain, nausea and vomiting.

Ten weeks prior to admission, on the morning following an evening of heavy eating, he suffered the first attack of biliousness and diffuse intermittent abdominal ache, nausea and vomiting. His physician treated him with belladonna and paregoric, and the symptoms disappeared after five days. The patient was well until ten days before admission, when similar symptoms occurred, and several days later he noted for the first time continuous aching pain in the left side of the abdomen. This was partially relieved when he vomited some "dark fluid."

X-ray studies at another hospital were said to have shown partial obstruction in the midportion of the small intestine, esophageal varices, a small liver shadow and diverticula in the lower portion of the descending colon. After these studies were made, the patient improved and remained well until twenty-four hours prior to admission to this hospital. At this time, two or three hours after eating, the usual symptoms of biliousness, nausea and abdominal ache recurred and were relieved by vomiting. The patient was symptomless on the day of admission. The vomitus had never contained blood, and there had been no changes in the stool characteristics.

The family history was irrelevant.

At seventeen years of age, the patient had peritonitis secondary to a perforated appendix, and this required drainage for seven weeks. Following this, he developed phlebitis in both legs, which had intermittently been swollen ever since. Thirteen years before entry, a sore left leg and hip developed. Soon after this, the patient had an attack of severe chest pain and dyspnea, interpreted as pulmonary infarction. The cardiorespiratory history was otherwise irrelevant.

The patient was said to have consumed four or more highballs each day. His diet included meat, milk and vegetables; however, he usually ate only one meal a day.

Physical examination revealed a well-developed and well-nourished man in no discomfort. Examination of the heart and lungs was negative. The veins over the upper and lower abdomen were prominent. No abdominal masses were felt, and there was no tenderness. Rectal examination was negative. There was slight edema of the left leg, and pigmentation of both lower legs.

The blood pressure was 118 systolic, 68 diastolic. The temperature was 99°F., the pulse 89, and the respirations 20.

Examination of the blood revealed a red-cell count of 4,000,000 with a hemoglobin of 78 per cent, and a white-cell count of 9500. Examination of the urine was negative.

On the second hospital day, soon after a meal of toast and coffee, the patient noticed the onset of slightly crampy midabdominal pain, which increased in severity during the day. The patient retched but was unable to vomit. Physical examination at this time was negative.

That evening, he vomited several hundred cubic centimeters of slightly green, watery material and obtained immediate relief. There was moderate diffuse tenderness, maximum to the right of the umbilicus, and spasm of the entire abdomen.

The patient vomited several times during the next day. The white-cell count was found to be 40,700 and, five hours later, 48,000. At this time, there was definite tenderness in the right upper quadrant, and operation was immediately performed.

## Differential Diagnosis

Dr. Reginald H. Smithwick: So far as I can see, there was no opportunity to take any x-ray films on this patient before he was operated on, at least in this hospital.

The picture given by the history is that of a well-nourished, middle-aged man who, aside from slight secondary anemia, appeared to be in good condition on entry to the hospital. The past history is important in that he had an operation for appendicitis, with drainage, twenty-seven years previously. There is evidence that this was followed by a deep thrombophlebitis, with exacerbation four years later. This might be the explanation for dilated veins over the lower chest and abdomen rather than cirrhosis of the liver resulting from indiscretions of eating and drinking. In any event, the relation of either an old deep thrombophlebitis or cirrhosis to the present illness is not clear.

The present illness consisted of four attacks of crampy, periumbilical pain, associated with nausea and vomiting over a ten-week period, the first lasting five days and the second a shorter period — being followed, however, by less severe, but rather persistent abdominal discomfort. The third attack was sudden and severe but of short duration, and the fourth was sudden in onset, with increasing severity, persistent nausea, tenderness, spasm and a striking rise in the white-cell count. No mention is made of distention or abnormal peristalsis. The nature, location and severity of the pain, coupled with the information from the x-ray examination elsewhere revealing partial obstruction, suggest that the lesion was located in the small intestine.

Other conditions that might possibly cause these symptoms are pancreatitis, disease of the biliary tract, with subsequent rupture of the gall bladder, possibly a perforated peptic ulcer, diverticulitis with perforation and appendicitis. Presumably, the appendix was removed twenty-six years previously, although one cannot be certain that that was so. Diverticulitis with perforation is rare, except in the sigmoid. No mention is made of fever, which should be considerable if the cause of the symptoms at the time of the operation was primarily an inflammatory process, although it is possible that peritonitis was present at the time of operation.

The most probable diagnosis is obstruction of the midportion of the small bowel, associated with interference of the blood supply. Mesenteric thrombosis might cause such a picture, but the pain is likelier to continue and does not explain four attacks in ten weeks, with spontaneous recovery from the first three. In view of the previous operation, partial obstruction from an adhesive band culminating in obstruction should be placed first as the cause of this man's difficulties. The symptoms, however, could be equally well explained by recurring intussusception related to tumor, polyp or stricture of the small bowel, resulting in necrosis of the invaginated bowel.

Dr. Leland S. McKittrick: Do you exclude an acute pancreatitis? You passed over that very quickly, Dr. Smithwick. Do you believe it is usually so easy to rule it out in such a case?

Dr. Smithwick: It seems to me that, with an acute pancreatitis, it is unusual to have so many attacks as this man had, although we do know that it can be recurrent. Acute pancreatitis simulating small-bowel obstruction, I believe, was the first disease mentioned in the differential diagnosis; it should be included. I should expect that more would have been said regarding the general serious condition of the patient, with more evidence of shock and collapse, and I should not expect the white-cell count to be so elevated as this man's was. It would be much lower in acute pancreatitis, and there would be a good deal more evidence of collapse than I gather from the clinical description in this case. I think acute pancreatitis is a very definite possibility, but I do not put it first.

Dr. Tracy B. Mallory: Does anyone want to hazard an opinion on the relation of the four highballs a day to the esophageal varices? That is a rather crucial figure.

Dr. McKittrick: I suppose that would depend on the highballs. Many people would believe that four a day would do it.

Dr. Aubrey O. Hampton: They said that he had a small liver, did they not?

Dr. Smithwick: I was rather inclined not to lay much stress on that because it seemed to be information that was obtained elsewhere and was not confirmed by evidence accumulated during the present illness.

Dr. McKittrick: I rather had the impression that obstruction had a much more abrupt and

more positive onset than this. I should be a little hesitant to expect strangulative obstruction, because of the past history. Also, the story of the last month alone would not fit into my concept of strangulated small-bowel obstruction, but I am probably being educated.

DR. SMITHWICK: So far as I can estimate from the history, in the course of twenty-four to thirty-six hours, this man passed from a healthy person to one who was desperately sick, with no mention of fever or other evidence of an inflammatory process. That seems quite abrupt and severe to me.

DR. MALLORY: The temperature on the first day was 99.5°F., and on the second 98°F.

DR. SMITHWICK: With increasingly severe pain of rather sudden onset, I gather from the description of the periumbilical crampy midline abdominal pain.

DR. MCKITTRICK: But not bad.

DR. SMITHWICK: Not bad at the moment it started, but increasingly severe, followed by generalized tenderness and spasm.

DR. REED HARWOOD: Did you ask if the esophageal varices and small liver could be linked with the present symptoms?

DR. MALLORY: No; but I should be interested if anyone had a theory by which they could be explained. What should you say, Dr. Hampton, about the reliability of the radiologist's observation of varices?

DR. HAMPTON: If the examination is carried out in a Grade A hospital by a Grade A man, the observations should be very accurate. I wager that this patient had cirrhosis of the liver, because I know who made the examination.

A PHYSICIAN: Dr. Fuller Albright had a patient with four attacks of pain simulating gallbladder disease and various other things who finally had a severe venous thrombosis of the small bowel.

DR. SMITHWICK: I was not aware that cirrhosis of the liver ever resulted in mesenteric venous thrombosis. If so, that would be a likely sequence of events in this case.

### PREOPERATIVE DIAGNOSIS

Gangrene of bowel.

### DR. SMITHWICK'S DIAGNOSIS

Obstruction of midportion of small bowel, with occlusion of its blood supply.

### ANATOMICAL DIAGNOSES

Mesenteric and portal thrombosis, recent.
Venous infarction of small intestine, acute.
Thrombosis of splenic vein, old.
Thrombosis of femoral and popliteal veins, old, bilateral.
Esophageal varices.
Splenomegaly, slight.
Peritonitis, acute.
Operative wound: appendectomy.

### PATHOLOGICAL DISCUSSION

DR. MALLORY: This patient was explored. When the abdomen was opened, the operator felt a mass that was surrounded by omentum. On peeling back the omentum, he found that the mass consisted of loops of discolored small intestine, about 150 cm. in length and matted together by fibrinous adhesions. All the veins in the mesentery leading from these loops were thrombosed. The surgeon, who also examined and felt the liver, reported that it was small and that it was finely granular and tough. He noted a very hard cord, which extended from somewhere near the hilum of the liver across the abdomen in the direction of the spleen, and suggested an old thrombosis of the splenic vein.

At autopsy, two days later, the latter observation proved to be entirely correct. There was complete obliteration of the splenic vein, obviously going back many years; it was completely organized and partially recanalized. The spleen was fibrotic, but not much enlarged. There were esophageal varices, but the liver seemed entirely smooth and softer than normal; microscopically, there was no cirrhosis. The acute thrombotic process in the mesenteric veins had, in the intervening two days, spread to involve the entire portal system. Every peripheral branch of the portal vein was thrombosed, as was the main portal vein, and the thrombi extended well up into the portal radicals of the liver. There were old and dense fibrous adhesions about the cecum in the region of the appendix, but none of the adhesions could have obstructed any loop of small bowel, so that we have nothing at autopsy to account for the intermittent attacks except the thrombotic process; accordingly, I think we must assume that the thrombosis had occurred in stages and did account for the recurring episode.

DR. MCKITTRICK: Warren and Eberhard* some years back, from a study of venous mesenteric thrombosis, concluded that one could have recurring episodes without necrosis of the bowel, many times culminating in episodes of this kind. The recurring multiple episodes in the past are entirely consistent with it.

DR. MALLORY: I had forgotten that. I suppose that it could occur with venous thrombosis but probably never with the arterial type of mesenteric thrombosis.

*Warren, S., and Eberhard, T. P. Mesenteric venous thrombosis. *Surg., Gynec. & Obst.* 61:102-121, 1935.

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## INDUSTRIAL MEDICINE IN MASSACHUSETTS

The announcement of the Committee on Industrial Health that appears elsewhere in this issue of the *Journal* focuses attention on the medical aspects of a dislocation in civil life that is of growing importance. The industrial expansion of the Nation is now of such proportions that it is said to be creating urgent problems in many areas. As yet, no one has actually conducted a survey with sufficient care to give an accurate picture, but it is well known that whole cities and towns for the sole purpose of wartime production are rapidly springing into existence. How quickly and how completely they may be provided with the civilized accoutrements of the older cities and towns in these days of shortages and priorities is an open question. Already, established cities and towns are learning that they must sacrifice many of the things they formerly considered essential, and these sometimes include medical services. For example, the Procurement and Assignment Service has not hesitated to classify the only physician in a small town as available when such a town is relatively close to others from which doctors can be obtained when needed. This and other comparable privations are beginning to create an appreciation of the immensity of the task. To what extent industrial demands, over and above the tremendous military needs, for medical service will still further deplete civilian resources remains to be seen, but it is both prudent and timely that steps are being taken to prepare for whatever dislocation becomes necessary.

In Massachusetts, the natural geography is such that large areas cannot be altogether remote from medical and hospital services. There are a larger number of both physicians and hospital beds per unit of population than in most other sections of the country, and expansion generally consists in the enlargement of previously existing plants or facilities. Furthermore, the State Department of Labor and Industries is well organized and alert, and its Division of Occupational Hygiene is nationally recognized as a leader in industrial medicine. And, finally, certain members of the State Department of Public Health are especially interested in the potentialities of industrial health. In other words, Massachusetts appears to be in a position to solve whatever problems arise, and to do this with already existing machinery. If so, she will be more fortunate than other states, where the resources are more meager and the load relatively greater.

During the early days of the late depression, President Ernest M. Hopkins, of Dartmouth College, insisted that times of stress and change were times of opportunity for those who could foretell and foresee the trends of the future. Not only did this prove to be so, but many who set their courses, not by foreseeing the future, but by mere

expediency, lived to reap the benefits of currently changing fortunes. In ordinary times, an expanding and medically minded industry would reach for a young physician — a man who could grow and mature with the business. Today, however, the opportunity is open to all. It is likely that those who have done best in private practice will do best in industrial practice, and this is fortunate because in Massachusetts the greatest opportunity lies in serving small plants, in which three quarters of the workers of the State are employed. The medical service for these small plants is almost certain to develop as a part-time activity of the practicing physician, rather than as a full-time assignment. This circumstance also places industrial medicine where it belongs — not in the group of specialties, but in the group of activities that constitute the general practice of medicine and surgery.

## VIRUS PNEUMONIA AND ORNITHOSIS

The atypical pneumonias of varying severity that fail to yield significant bacteriologic agents and also fail to show the characteristic favorable response to sulfonamide drugs continue to be a challenge to physicians and laboratory investigators. At present, the group may be said to constitute a fairly well-defined clinical syndrome. The meager positive results of laboratory studies, however, have already pointed to the diversified character of the etiologic agents in cases that present very similar clinical findings. The situation is probably analogous to that found in primary lobar pneumonia, which is now known to consist of a group of specific infectious diseases caused by many organisms, of which certain types of pneumococci are the most frequent.

The possible significance of the rickettsia of Q fever and of the virus that Weir and Horsfall encountered when they used the mongoose for the study of materials from human cases has already been discussed in the *Journal*.* Intensive work on this problem is continuing in a number of laboratories throughout the country, and also by groups of investigators in the Army and Navy. The present status of the problem is summarized in this and the preceding issue of the *Journal*.

Two important points brought out in these reports are worth emphasizing. The first concerns terminology. The diagnosis "virus pneumonia" is now widely used both in verbal discussions and in many written reports, in spite of the failures to demonstrate filterable viruses in almost all the cases so labeled. Many writers, to avoid this possibly misleading designation, have resorted to the use of a number of terms, each of which emphasizes some clinical, roentgenologic or, sometimes, pathologic feature of the disease. For purposes of classification, however, there are serious objections to such terminology. The designation recently recommended to the Surgeon General for use in the United States Army is, "*primary atypical pneumonia, etiology unknown*," and this seems to be the most suitable one suggested thus far. It implies that an earnest effort has been made to rule out the known etiologic agents, particularly bacteria. It also implies that the known nonbacterial causes of similar respiratory infections, such as influenza, psittacosis and Q fever, have been considered and that they were either ruled out or thought to be unlikely causes on clinical or epidemiologic grounds.

The second point of interest is the increasing number of reports of the finding of a psittacosis-like virus in some cases of this group, as well as the association of these cases with pigeons and domestic fowl. The studies of a number of workers, including Meyer, Pinkerton, Francis, Eaton and their collaborators, have indicated that the virus concerned is very widespread among the pigeons in this country wherever it has been sought. It has been isolated from a significant number of birds in many pigeon lofts, and serologic studies have indicated very widespread latent and subclinical infection. Furthermore, evidence of infection has been found in the pigeons

*Editorial. Virus pneumonia and Q fever. *New Eng. J. Med.* 224:36, 1941.

in Central Park and in other parts of New York City.

Cases of atypical pneumonia, clinically similar in all respects to those described by many writers, have occurred in pigeon breeders and also in persons having contact with ordinary street pigeons. Serologic evidence of infection has also been found in many pigeon breeders who have had no clinical symptoms. Infections, both latent and manifest, have been observed in barnyard fowl, including chickens, ducks and turkeys, but not in wild birds, and cases ascribable to contact with sick fowl have also occurred.

Meyer has suggested that such infections be called "ornithosis" and that the atypical pulmonary infections associated with them be termed "ornithotic pneumonia." Thus, another group of cases of atypical pneumonia has been removed from the category of "etiology unknown." The diagnosis may be established by the demonstration of the virus by means of mouse inoculation of sputum or lung material obtained at the height of the disease; or infection with the virus may be demonstrated by an increase in the titer of antibodies by complement-fixation tests for the virus during convalescence. There are some difficulties involved in both methods because of the close immunologic relation between the psittacosislike virus of pigeons and certain naturally occurring viruses of mice, as well as the virus of lymphogranuloma venereum. Since subclinical infection with the last virus has been demonstrated recently, this difficulty is more than merely theoretical.

It should be borne in mind, however, that the number of human cases of atypical pneumonia in which the pigeon virus has been demonstrated either by direct isolation or by immunologic tests is still very small in comparison with the number of cases in which it has been sought. In many, if not most, proved cases, a history of contact with pigeons, and often with sick ones, could be elicited. In the great majority of cases of characteristic atypical pneumonia, the etiology still remains unknown. It is hoped that the intensive studies now in progress will remove a greater proportion of these cases from this category and place them in the group of cases with known etiology.

## MEDICAL EPONYM

### Von Recklinghausen's Disease

This disease forms the subject matter of a monograph by Friedrich Daniel von Recklinghausen (1833–1910), professor at Strassburg, entitled *Über die multiplen Fibrome der Haut und ihre Beziehung zu den multiplen Neuromen* [*Multiple Fibromas of the Skin and Their Relation to Multiple Neuromas*] (Berlin, 1882), which appeared as a part of the *Festschrift* commemorating the twenty-fifth anniversary of the foundation of the Pathological Institute in Berlin and dedicated to Rudolf Virchow. A portion of the translation follows:

> From the results of these studies, I may assert that these little tumors are fibromas, which are formed in the small nerves of the skin after the same fashion as the fibromas in the larger trunks. . . . In respect to their origin, the *multiple, soft fibromas of the skin* have arisen from neuromas, hence *neuromatous fibromas* or *neurofibromas.*

R. W. B.

## MASSACHUSETTS MEDICAL SOCIETY

### COMMITTEE ON INDUSTRIAL HEALTH

Following the announcement that called attention to the distribution of the *Manual on Industrial Health for Defense* in the July 30 issue of the *Journal*, the Committee on Industrial Health received several inquiries from physicians seeking openings in industrial medicine. Because the committee had no ready method of meeting these inquiries, on August 17, it voted to "constitute itself as an agency to gather what information it can concerning doctors who may be available for industrial work and also information concerning possible placements for such doctors, working, of course, in close co-operation with the Procurement and Assignment Service and with due regard for other than industrial need for medical service."

If this function is to be developed, it will be necessary for the committee to possess certain information concerning physicians who are ready to undertake industrial practice. The committee is therefore preparing a registration form that will be forwarded to any Massachusetts physician who wishes to record himself or herself as a candidate

for industrial assignment, as well as to state the conditions under which he or she would be willing to accept such an assignment. The committee may be addressed for this purpose at 8 Fenway.

DWIGHT O'HARA, *Chairman*

## COMMITTEE ON MATERNAL WELFARE

### CASE HISTORY: GONOCOCCAL SEPTICEMIA, PELVIC PERITONITIS AND THROMBOPHLEBITIS, FOLLOWED BY LAPAROTOMY AND DEATH

In a twenty-nine-year-old primipara who had been treated intelligently and adequately during her pregnancy, labor was induced by rupture of the membranes two weeks from term because of mild toxemia, a blood pressure of 160 systolic, 110 diastolic, and slight albuminuria. The past history was irrelevant. Labor started immediately after the membranes had been ruptured and progressed normally to full dilatation. The patient was delivered by low forceps because of the prolonged second stage and because of maternal fatigue. The third stage was complicated not by hemorrhage but by the fact that the placenta did not separate. During the first twenty-four hours after delivery, several 1-cc. doses of pituitary extract were given to stimulate separation of the placenta. Because this did not accomplish separation, the uterus was invaded manually under very strict asepsis, the line of cleavage between the placenta and the uterine wall readily found, and the placenta and membranes manually delivered intact. There was no hemorrhage during or following this procedure. A chill followed within the first twenty-four hours after delivery of the placenta, a septic temperature developed, and in spite of repeated transfusions and chemotherapy the patient died two weeks later. Gram-negative intracellular diplococci were found in a smear from the cervix, and repeated gonococcal-fixation tests were reported positive. Two days before death, a laparotomy was undertaken for the purpose of draining a pelvic abscess. Autopsy showed general septicemia, pelvic cellulitis, acute pelvic peritonitis, thrombophlebitis of the right common iliac vein and an infarct in the right lung.

*Comment.* The operative conduct of this case cannot be criticized. Induction of labor by rupture of the membranes during the last month of pregnancy, in the presence of increased blood pressure and albuminuria, is certainly advisable treatment. The fact that labor immediately followed rupture of the membranes shows that the cervix was favorable for induction. The delayed second stage had no necessary connection with this induction. The question of leaving a placenta in situ for twenty-four hours or longer after the birth of the baby is a problem that is treated differently in various clinics. In the absence of hemorrhage, it should certainly be safe to leave the placenta as long as it was left in this case before manual removal is attempted. It is logical to conclude that in patients of this sort who do not bleed after delivery the placenta has remained entirely attached. It is in cases in which partial attachment and partial separation occur, accompanied by free hemorrhage, that the placenta must be immediately attended to. In this case, the uterus was invaded under strictest asepsis for the purpose of making a diagnosis. This might have been a completely adherent placenta and one that was an accreta, which could not have been removed manually. The diagnosis of this condition can be made only by intrauterine manipulation. Had a placenta accreta been diagnosed, the treatment would have been transfusion and hysterectomy. In this case, since there was apparently no bleeding during or following the operation and since a line of cleavage was easily recognized, the placenta was a mildly adherent one. Because gonococci were isolated in a smear from the cervix and gonococcal-fixation tests were positive during convalescence, the bacteriologic cause of the infection is demonstrated beyond argument. The trauma of removing this placenta may well have been a contributing factor. There is nothing to commend the laparotomy that preceded this death by two days. Had a pelvic abscess been apparent, it should have been drained posteriorly.

## DEATH

JACOBY — RUDOLPH JACOBY, M.D., of Newtonville, died August 20. He was in his fifty-third year.

Born in Newburyport, Dr. Jacoby received his degree from Boston University School of Medicine in 1911. He was professor of dermatology and syphilology at Boston University School of Medicine, and was a member of the American Academy of Dermatology and Syphilology and the New England Dermatological Society, and a fellow of the Massachusetts Medical Society and the American Medical Association.

His widow and two sons survive him.

## MISCELLANY

### NOTE

The Medical Library Association held its forty-fourth annual meeting in New Orleans on May 7–9, 1942. The officers elected for the coming year are as follows: Mary Louise Marshall (Tulane University), president; Dr. John F. Fulton (Yale University), vice-president; Frida Pliefke (Mayo Clinic), secretary; and Bertha B. Hallam (University of Oregon), treasurer.

*(Notices on page viii)*

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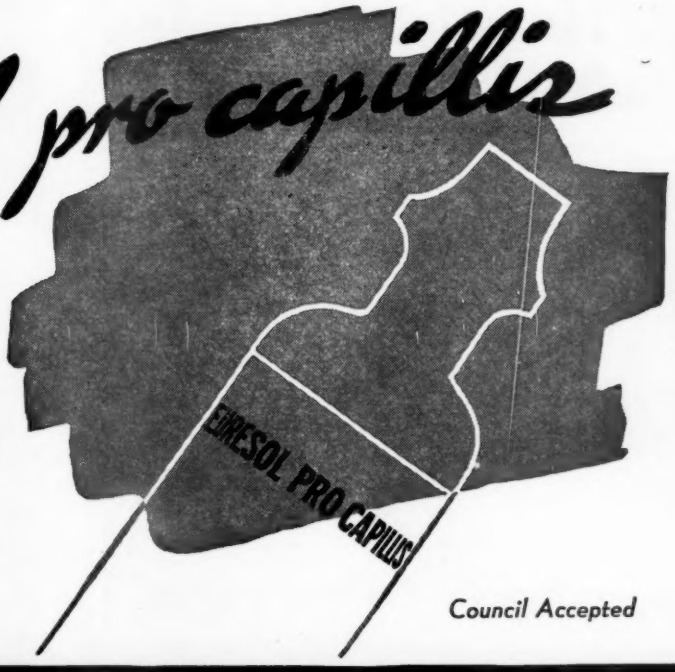


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## NOTICES

### REMOVAL

Dr. James F. Conway, 464 Commonwealth Avenue, Boston, announces the removal of his office September 1, to 1101 Beacon Street, Brookline, LONgwood 8144.

### SOCIETY MEETINGS AND CONFERENCES

Calendar of Boston District for the Week Beginning Sunday, September 6

Monday, September 7

12:15–1:15 p.m. Clinicopathological conference. Peter Bent Brigham Hospital amphitheater.

Tuesday, September 8

12:15–1:15 p.m. Clinicoroentgenologic conference. Peter Bent Brigham Hospital amphitheater.

Wednesday, September 9

*12:00 m. Clinicopathological conference. Children's Hospital.

*Open to the medical profession.

September 9–12. American Congress of Physical Therapy. Page x, issue of May 14.

September 29, 30 and October 1. Connecticut Clinical Congress. Yale Law School Building, New Haven, Connecticut.

September 30–October 10. Conference and Course in Legal Medicine. Mallory Institute of Pathology, Boston City Hospital. Page ix, issue of July 23.

October 7–December 23. Yale University School of Medicine. Page 362, issue of August 27.

October 12–23. 1942 Graduate Fortnight. New York Academy of Medicine. Page xi, issue of May 21.

October 14–17. American Academy of Physical Medicine. Hotel Statler, Boston.

October 19–23. 1942 Clinical Congress of the American College of Surgeons. Page ix, issue of February 5.

October 21–24. Conference on Venereal-Disease-Control Needs in Wartime. Page ix, issue of August 20.

November 17–20. American College of Surgeons. Page ix, issue of August 20.

February 13. American Board of Obstetrics and Gynecology. Page ix, issue of July 2.

April 12–16. American College of Physicians. Page x, issue of July 16.

### District Societies

BRISTOL SOUTH

December 3. Fall River.
May 6. New Bedford.

FRANKLIN

September 8.
November 10.
January 12.
March 9.
May 11. Annual meeting.

All meetings are held at 11:00 a.m. at the Franklin County Hospital, Greenfield.

HAMPSHIRE

September 9.
November 4.
January 6.
March 3.
May 5.

MIDDLESEX NORTH

October 28.
January 27.
April 28.
July 28.

PLYMOUTH

October 15. Moore Hospital.
November 19. Plymouth County Hospital.
January 21. Brockton Hospital.
February 18. Jordan Hospital, Plymouth.
March 18. Goddard Hospital.
April 15. Bridgewater State Farm.
May 20. Lakeville.

WORCESTER
SEPTEMBER 9. Belmont Hospital, Worcester.
OCTOBER 14. Rutland State Sanatorium, Rutland.
NOVEMBER 11. Grafton State Hospital, North Grafton.
DECEMBER 9. Worcester City Hospital, Worcester.
JANUARY 13. St. Vincent Hospital, Worcester.
FEBRUARY 10. Worcester State Hospital, Worcester.
MARCH 10. Memorial Hospital, Worcester.
APRIL 14. Hahnemann Hospital, Worcester.
MAY 12. Annual meeting.

WORCESTER NORTH
OCTOBER 28.
JANUARY 27.
APRIL 28.
JULY 28.

## BOOKS RECEIVED

**The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.**

*Cabot and Adams Physical Diagnosis.* By F. Dennette Adams, M.D., instructor in medicine, Courses for Graduates, Harvard Medical School, and physician, Massachusetts General Hospital. 8°, cloth, 888 pp., with 399 illustrations. Baltimore: The Williams and Wilkins Company, 1942. $5.00.

*Treatment in General Practice.* By Harry Beckman, M.D., professor of pharmacology, Marquette University School of Medicine, Milwaukee, Wisconsin. Fourth edition, thoroughly revised. 4°, cloth, 1015 pp., with 20 tables, 1 chart and 5 illustrations. Philadelphia: W. B. Saunders Company, 1942. $10.00.

*Stedman's Practical Medical Dictionary.* Fifteenth revised edition, with etymologic and orthographic rules. By Stanley T. Garber, M.D., University of Cincinnati College of Medicine. 8°, cloth, 1257 pp. Baltimore: The Williams and Wilkins Company, 1942. $7.50.

*The Pathology of Trauma.* By Alan R. Moritz, M.D., professor of legal medicine, Harvard Medical School, lecturer in legal medicine, Tufts College Medical School, lecturer in legal medicine, Boston University School of Medicine, pathologist, Massachusetts State Department of Public Safety, consulting pathologist, Massachusetts State Department of Mental Health, and associate medical examiner, Suffolk County. 8°, cloth, 386 pp., with 117 illustrations. Philadelphia: Lea and Febiger, 1942. $6.00.

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